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Paying for Unapproved Medical Products

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PAYING FOR UNAPPROVED MEDICAL PRODUCTS

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This symposium article examines the use of investigational (unapproved) medical products in the United States, with particular focus on who pays for this use. In the United States, the question of who pays for the use of approved medical products for their intended indications is complicated enough, with some expenses borne by private payers, some by public payers, some covered as charity care, and some paid out of pocket by patients.[1] A separate question is off-label use, in which an approved medical product is used for an unapproved indication.[2] In this article, we focus on a narrower issue: what entities in the United States pay for access to unapproved medical products, e.g., investigational drugs, devices, or diagnostics that have not (yet) received Food and Drug Administration ("FDA") approval.

We examine the various forms of preapproval access ("PAA") to experimental medical products available in the United States—clinical trials and non-trial preapproval access via the Expanded Access ("EA") and Right to Try ("RTT") pathways. For each, this paper analyzes which entity—individual, insurer, sponsor, or

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1. COMM. ON THE CONSEQUENCES OF UNINSURANCE, INST. OF MED. OF THE NAT'L ACADS., HIDDEN COSTS, VALUES LOST: UNINSURANCE IN AMERICA 38 (2003), http://www.nap.edu/catalog/10719.html.

2. *Off-Label Drug Use*, AM. CANCER SOC'Y, https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/off-label-drug-use.html (last revised Mar. 17, 2015).

other—bears the cost and what limitations or caps, if any, exist on these costs. This paper considers various proposed novel payment mechanisms that may permit more equitable use of investigational medical products.

This analysis grapples with the ongoing tension between the desire to make access widely available to those for whom such products provide a last hope and the concern that allowing the purchase of unapproved medical products in the same manner as approved medical products likely would have negative consequences for individual patients, public health, payers, and those who support payers through premiums and taxes, in a healthcare system already grappling with scarcity and inequity.[3]

The vast majority of treatments-in-development ultimately do not receive regulatory approval because they are determined via clinical trials to be unsafe and/or ineffective.[4] Thus, the issue of paying for investigational medical products is intertwined with both the risk of harm to patients, which in turn can lead to expensive follow-up care, and the risk of wasteful expenditure on products that simply do not work.[5] Moreover, in a world of scarce resources, it must be decided to what extent access to investigational medical products is a priority worthy of the subsequent opportunity costs. Also, if manufacturers are allowed to profit indefinitely from unapproved products without completing the pivotal trials necessary to gain marketing authorization, the medical, payer, and patient communities may never learn whether the product is safe, effective, or worth its price.[6] This has implications as well for future treatments, which would likely be tested against the unproven product, a practice that has become standard of care in light of the lack of other options.

Part I outlines payment-related disparities in access ingrained in the current United States healthcare system. Part II focuses on access in the context of clinical trials, which most payers

3. *Unapproved Drugs*, U.S. FOOD & DRUG ADMIN. (Jan. 29, 2020), https://www.fda.gov/drugs/enforcement-activities-fda/unapproved-drugs.

4. Joseph DiMasi, *Pharmaceutical R&D Performance by Firm Size: Approval Success Rates and Economic Returns*, 21 AM. J. THERAPEUTICS 26, 26 (2014).

5. Gail A. Van Norman, *Expanding Patient Access to Investigational Drugs: Single Patient Investigational New Drug and the "Right to Try"*, 3 J. AM. COLL. CARDIOLOGY 280, 288 (2018).

6. *See* Christopher Robertson & Victor Laurion, *Tip of the Iceberg II: How the Intended-Uses Principle Produces Medical Knowledge and Protects Liberty*, 11 N.Y.U. J.L. & LIBERTY 770 (2017).

have begun to cover, but where remaining uncovered expenses can disincentivize participation in clinical trials, even among those highly motivated to enroll. Part III discusses non-trial preapproval access pathways, specifically Expanded Access and Right to Try, where coverage is scant. Part IV briefly deals with investigational products (such as stem cell treatments) that are available via unregulated or underregulated direct-to-consumer sales. Part V then reviews the ethical considerations inherent in paying for investigational medical products.

I. THE U.S. HEALTHCARE SETTING

In the United States, prior to broad release of a new medical product, a manufacturer must produce a reasonable amount of evidence about the product's safety and efficacy and secure approval by the FDA.[7] Thus, "unapproved" or "investigational" refers to products that the FDA has not approved for prescription, sale, and marketing. In most circumstances, patients access such medical products by participating in clinical trials.[8]

However, for severely ill patients who are unable to join clinical trials and who have no other treatment options, use of these products is available through a variety of access programs in many countries.[9] These programs vary in detail, and they utilize different terminologies, e.g., Expanded Access or Right to Try in the United States; Special Access Program in Canada; and Temporary Authorisation for Use in France, among others.[10] Regardless of the terminologies, these mechanisms share a common goal of permitting seriously or terminally ill patients with no other therapeutic options to use unapproved medical products in hopes of potential therapeutic benefit.[11]

7. Christopher Robertson, *When Truth Cannot be Presumed: The Regulation of Drug Promotion Under an Expanding First Amendment*, 94 B.U. L. REV. 545, 547 (2014).

8. *Compassionate Drug Use*, AM. CANCER SOC'Y, https://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/compassionate-drug-use.html (last revised Nov. 19, 2018).

9. *Id.*

10. VANESSA PLATE, THE IMPACT OF OFF-LABEL, COMPASSIONATE AND UNLICENSED USE ON HEALTH CARE LAWS IN PRESELECTED COUNTRIES 34 (2010).

11. *See* Gayarthri Balasubramanian et al., *An Overview of Compassionate Use Programs in the European Union Member States*, 5 INTRACTABLE & RARE DISEASES RES. 244 (2016) (explaining programs in European Union member countries that allow patients to access drugs without participating in clinical trials); Jonathan Jarow et al., *Overview of FDA's Expanded Access Program for Investigational Drugs*, 51 THERAPEUTIC INNOVATION & REG. SCI. 177 (2017)

Patient demand for investigational medical products in the United States has increased in the last several years, likely in response to heightened media and political attention to the topic, coupled with widespread frustrations about access to medicines even after regulatory approval and longstanding perceptions by some that drug development is too slow and insufficiently patient-centric.[12]

We focus on the United States, where access to healthcare is fundamentally unequitable. For example, recent news reports detail situations in which patients have been denied transplants due to concerns that they cannot afford post-transplant medications necessary to prevent rejection of the donated organ;[13] patients are unable to afford the ongoing expense of insulin and ration it at the risk of death or other preventable harm;[14] and patients are discharged even though continued hospitalization is warranted.[15]

Healthcare coverage in the United States is fragmented, with the largest group of Americans insured through their employers' contracts with private payers.[16] Americans who receive publicly-funded insurance do so primarily through two programs: Medicare (intended primarily for individuals over the age of sixty-five) and Medicaid (intended primarily for low-income individuals).[17]

There have been numerous proposals for achieving universal insurance coverage, either through a single-payer system or a

(describing the FDA's Expanded Access program, which allows patients to access unapproved drugs without participating in clinical trials); Laura L. Kimberly et al., *Pre-approval Access Terminology: A Cause for Confusion and a Danger to Patients*, 51 THERAPEUTIC INNOVATION & REG. SCI. 494 (2017) (clarifying terms); Eline M. Bunnik et al., *Little to Lose and No Other Options: Ethical Issues in Efforts to Facilitate Expanded Access to Investigational Drugs*, 122 HEALTH POL'Y 977 (2018) (surveying issues).

12. Kelly Folkers et al., *Federal Right to Try: Where is it Going?*, 49 HASTINGS CTR. REP. 26, 29 (2019).

13. JoNel Aleccia, *No Cash, No Heart. Transplant Centers Require Proof of Payment*, KAISER HEALTH NEWS (Dec. 5, 2018), https://khn.org/news/no-cash-no-heart-transplant-centers-require-proof-of-payment.

14. Ed Silverman, *One-Quarter of People with Diabetes in the U.S. are Rationing Their Insulin*, STATNEWS (June 18, 2019), https://www.statnews.com/pharmalot/2019/06/18/one-quarter-of-people-with-diabetes-in-the-u-s-are-rationing-their-insulin.

15. MARTIN CASTRO ET AL., U.S. COMM. ON CIVIL RIGHTS, PATIENT DUMPING iv (2014), https://www.usccr.gov/pubs/docs/2014PATDUMPOSD_9282014-1.pdf.

16. EDWARD R. BERCHICK ET AL., U.S. CENSUS BUREAU, HEALTH INSURANCE COVERAGE IN THE UNITED STATES: 2017 2 (2018), https://www.census.gov/content/dam/Census/library/publications/2018/demo/p60-264.pdf.

17. James McWhinney, *Medicare vs. Medicaid: What's the Difference?*, INVESTOPEDIA (Apr. 15, 2020), https://www.investopedia.com/articles/pf/07/medicare-vs-medicaid.asp.

public option.[18] Yet, even with recent increases in coverage, many Americans remain uninsured or underinsured.[19] According to the most recent data issued by the United States Census Bureau in 2017, approximately 28.5 million individuals remain uninsured.[20] Approximately 43.8 million individuals are underinsured, meaning their insurance plans are inadequate to cover the medical products and services they need.[21] Instances in which insured patients are denied access to high-cost, but approved, treatments, such as gene therapies, have increasingly come to light.[22] Thus, access to unapproved products, where safety and efficacy have not been proven, must be seen in the light of these broader scarcities and inequities.[23]

II. CLINICAL TRIALS

Clinical trials are studies of interventions to ascertain reliable information about their safety and efficacy in treating a particular indication.[24] Human trials of new medical products proceed through three phases, from small studies to determine appropriate dosage levels, to larger, often randomized, studies of patients with the disease needing treatment.[25] In some Phase I studies, research subjects are healthy volunteers, and their participation is typically financially compensated.[26] But for most trials, participants are

18. Margot Sanger-Katz, *The Difference Between a 'Public Option' and 'Medicare for All'? Let's Define our Terms,* THE N.Y. TIMES (Feb. 19, 2019), https://www.nytimes.com/2019/02/19/upshot/medicare-for-all-health-terms-sanders.html.

19. BERCHICK ET AL., *supra* note 16, at 1.

20. *Id.* at 1.

21. Sara R. Collins et al., *Health Insurance Coverage Eight Years After the ACA*, COMMONWEALTH FUND (Feb. 7, 2019), https://www.commonwealthfund.org/ publications/issue-briefs/2019/feb/health-insurance-coverage-eight-years-after-aca. *See generally* CHRISTOPHER T. ROBERTSON, EXPOSED: WHY OUR HEALTH INSURANCE IS INCOMPLETE AND WHAT CAN BE DONE ABOUT IT (2019).

22. James Paton, *Gene Therapy Was Hailed as a Revolution. Then Came the Bill*, BLOOMBERG (Apr. 7, 2019, 9:00 PM), https://www.bloomberg.com/news/articles/2019-04-07/gene-therapy-was-hailed-as-a-revolution-then-came-the-bill.

23. Holly Fernandez Lynch & Alison Bateman-House, *Facilitating Both Evidence and Access: Improving FDA's Accelerated Approval and Expanded Access Pathways*, 48 J.L Med. & Ethics 365 (2020).

24. *Clinical Trials: What are Clinical Trials and Studies?*, NAT'L INST. ON AGING (Apr. 9, 2020), https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies.

25. *Id.*

26. *Id.*

patients who fit the eligibility criteria of a specific study with regard to disease or condition.[27]

Patients sometimes view participation in a clinical trial as a way to receive medical treatment;[28] however, the primary intent of clinical research is to learn about a new medical product and to evaluate its safety and efficacy in a specific patient population, rather than to provide treatment.[29] Even in the case of a negative finding, the trial contributes to scientific knowledge, provided the trial data and results are made public. This mix of possible individual benefit and societal benefit plays a role in how clinical trial-related expenses will be covered.[30]

A. Sponsors

In the United States, pharmaceutical or biotechnology companies sponsor the majority of clinical trials.[31] The trial sponsor often covers the costs of the investigational product and trial-required interventions and makes them available free of charge to the research subject/patient.[32] The sponsor's trial budget includes the provider and facilities fees for study-required visits or tests, along with any incentive payments or reimbursements trial participants may receive.[33] However, not all clinical trials involve experimental agents. A trial might test various approved drugs or combinations of approved drugs; in these cases, patients' insurers may pay costs the sponsor does not cover, as use of these drugs is part of standard medical care, despite their delivery in the context of a trial.[34] Expenses resulting from the trial that are not part of the trial

27. *Id.*

28. *Id.*

29. *Id.*

30. *Paying for Clinical Trials*, ONCOLINK (Sept. 17, 2018), https://www.oncolink.org/cancer-treatment/clinical-trials/paying-for-clinical-trials.

31. Michelle Llamas, *Big Pharma's Role in Clinical Trials*, DRUGWATCH (May 14, 2019), https://www.drugwatch.com/featured/clinical-trials-and-hidden-data.

32. *Clinical Trials: Sponsors and Sponsor-investigators*, MARS (Oct. 17, 2012), https://learn.marsdd.com/article/clinical-trials-sponsors-and-sponsor-investigators.

33. Kunal Sampat, *Ultimate Guide to Clinical Trial Costs*, CLINICAL TRIAL PODCAST (Jan. 21, 2017), https://clinicaltrialpodcast.com/ultimate-guide-to-clinical-trial-costs.

34. *Insurance Coverage of Clinical Trials*, AM. SOC'Y OF CLINICAL ONCOLOGY, https://www.asco.org/research-guidelines/clinical-trials/insurance-coverage-clinical-trials (last visited June 12, 2020).

protocol—for example, research-related injuries—are handled inconsistently.[35]

Aside from what sponsors may *pay*, another question is what they may *charge* patients for participation in a clinical trial. Since 1987, clinical trial sponsors have been permitted to charge patients for the provision of investigational medical products provided under an investigational new drug application ("IND"), but these costs can only include direct costs of manufacturing, shipping, and/or handling.[36]

Sponsors of INDs must request authorization from the FDA to charge for the use of an investigational medical product under that IND.[37] The FDA subsequently determines whether the sponsor may charge, but the agency does not determine *how* to carry out this charging.[38] Specifically for clinical trials, sponsors must provide evidence to the FDA that the investigational medical product under its IND has potential clinical benefit that, if demonstrated, would provide significant advantages for patients; that the data obtained from the trial is necessary for the product's approval submission and/or label expansion; and that the sponsor cannot conduct the clinical trial without charging.[39] The sponsor must also provide a document to the FDA that supports its calculation for cost recovery, and an independent certified public accountant must verify the accuracy of the calculations.[40] Finally, sponsors can charge for

35. Carolyn Riley Chapman et al., *The Quest for Compensation for Research-Related Injury in the United States: A New Proposal*, 47 J.L. MED. & ETHICS 732, 732 (2019).

36. FOOD AND DRUG ADMIN., U.S. DEPT. OF HEALTH & HUM. SERV., CHARGING FOR INVESTIGATIONAL DRUGS UNDER AN IND — QUESTIONS AND ANSWERS: GUIDANCE FOR INDUSTRY 8 (June 2016) https://www.fda.gov/media/85682/download [hereinafter GUIDANCE FOR INDUSTRY]. Under federal law, investigational new drugs cannot be shipped across state lines. Investigational New Drug (IND) Application, U.S. FOOD & DRUG ADMIN. (Jan. 22, 2020) https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application. Since sponsors of clinical trials will likely want to ship their product across state lines for the purposes of setting up additional trial sites, they must apply for an exemption to this federal requirement. *Id.* An investigational new drug application (IND) allows sponsors to ship investigational medical products across state lines and serves as a legal exemption to the federal regulations surrounding interstate commerce of investigational medical products. *Id.*

37. GUIDANCE FOR INDUSTRY, *supra* note 36, at 2.

38. *Id.* at 3. For example, a sponsor may contract with a third party or contract research organization that administers the trial or expanded access program. In this case, the FDA does not have authority to determine how that third party carries out charging patients. *Id.*

39. *Id.*

40. *Id.*

"extraordinary costs" if there are such factors like manufacturing complexity, scarcity of a necessary natural resource needed to produce the investigational medical product, a large quantity of product needed, or some combination of these circumstances.[41]

More recently, there has been a gradual introduction of so-called "pay-to-play" (or, more neutrally, "participant-funded") trials, in which the trial-related costs are borne by the research participant instead of a sponsor.[42] The U.S. Health and Human Services Secretary's Advisory Committee on Human Research Protections ("SACHRP") recently released a series of recommendations on pay-to-play studies.[43] These recommendations suggested that sponsors avoid charging participants but provide guidance and ethical considerations for doing so when there are legitimate reasons.[44] Others have commented on the ethical permissibility, or in some cases obligation, to reimburse and/or compensate clinical trial participants for completing a study.[45]

B. Patients/Caregivers

While most clinical trials provide investigational medicines for free, some may charge patients for ancillary costs, including office visits, lab tests, and imaging, which the patients' insurance—if they are insured—may or may not cover.[46] Patients or their caregivers may incur trial-related expenses, particularly for such costs as travel, parking, lodging, childcare, etc.[47] These issues have received increased attention in recent years. SACHRP produced guidance clarifying that such payments are ethically appropriate and do not

41. *Id.* at 4.

42. Rebecca Robbins, *Amid Rising Concern, Pay-to-Play Clinical Trials are Drawing Federal Scrutiny*, STATNEWS (Aug. 6, 2019), https://www.statnews.com/2019/08/06/amid-rising-concern-pay-to-play-clinical-trials-are-drawing-federal-scrutiny.

43. *Attachment A - Addressing Ethical Concerns Regarding Offers of Payment to Research Participants*, HHS, https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html (last reviewed Oct. 2019).

44. *Id.*

45. Emily Largent & Holly Fernandez Lynch, *Paying Research Participants: The Outsized Influence of "Undue Influence"*, 39 IRB: ETHICS & HUM. RES. 1, 1 (2017).

46. *Insurance Coverage and Clinical Trials*, NAT'L CANCER INST. (Feb. 6, 2020), https://www.cancer.gov/about-cancer/treatment/clinical-trials/paying/insurance.

47. Anna Lee, Kanan Shah & Fumiko Chino, *Assessment of Parking Fees at National Cancer Institute–Designated Cancer Treatment Centers*, JAMA ONCOLOGY (forthcoming 2020); *Calculating the Costs of Clinical Trials*, ASH CLINICAL NEWS (Dec. 1, 2019), https://www.ashclinicalnews.org/spotlight/feature-articles/calculating-costs-clinical-trials.

constitute undue manipulation of research subjects.[48] Well-funded pharmaceutical companies may cover these ancillary expenses, including logistical costs like travel and lodging, as part of the overall cost of conducting a clinical trial, but small pharmaceutical and biotechnology companies cover these costs less frequently.[49]

In contrast to trials initiated by biopharmaceutical companies, another category of trials is "investigator-initiated research."[50] In such cases, where physician-scientists run their own trials, researchers may be able to get the investigational product paid for by research funding or donated by its manufacturer, but incidental costs are even less likely to be covered.[51]

When patients are exposed to trial costs, those expenses may prevent patients who would be inclined to participate from doing so.[52] In the field of oncology, scholars have defined "financial toxicity" as the phenomenon of healthcare costs causing stress, bankruptcy, and worse health outcomes for patients.[53] Recently, scholars have focused this concept on clinical trials in particular, arguing that financial exposures may be one reason that clinical trials tend to disproportionately enroll whiter and wealthier populations, excluding those less able to pay trial-related expenses out of pocket.[54]

Some patients call upon others to assist with trial-related expenses. A case in point is that of Lily, "a bright and bubbly 13 year old" in England, whose family is seeking to enroll her in a United States-based clinical trial in Seattle, Washington.[55] According to a "crowdfunding"—the practice of soliciting a large number of small

48. *Attachment A - Addressing Ethical Concerns Regarding Offers of Payment to Research Participants*, HHS, https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html (last reviewed Oct. 2019).

49. Amit Pratap Singh Rathore, *Getting a Handle on Clinical Trial Costs*, CLINICAL LEADER (Apr. 25, 2019), https://www.clinicalleader.com/doc/getting-a-handle-on-clinical-trial-costs-0001.

50. R. Romanchuk, *The Noble Pursuit of Investigator-Initiated Research*, ADVARRA (June 19, 2019), https://www.advarra.com/investigator-initiated-research.

51. *Id.*

52. *Clinical Trials for Cancer Patients*, GOFUNDME (Apr. 14, 2020), https://www.gofundme.com/c/blog/clinical-trials-cancer-patients.

53. Fumiko Chino & S. Yousuf Zafar, *Financial Toxicity and Equitable Access to Clinical Trials*, 39 ASCO EDUC. BOOK 11 (2019).

54. *Id.*

55. Ellis Whitehouse, *Lily Wythe Gets 300k in Donations Thanks to One Pound Warriors Campaign*, ECHONEWS (Jan. 24, 2020), https://www.echo-news.co.uk/news/18184265.lily-wythe-gets-300k-donations-thanks-one-pound-warriors-campaign.

donations from individuals on the Internet[56]—campaign established for Lily on November 18, 2019, "a years [sic] treatment in the US . . . will cost around £300,000. This includes the cost of the trial, accommodation, flights and medical treatment she may need while she's there."[57] As a resident of Great Britain, Lily likely would not qualify for publicly funded insurance in the United States; thus, it would fall to her parents to either obtain private insurance (either by purchasing it or via an employer) or to pay for her expenses themselves.[58]

C. Private Payers

Based on contracts and policy documents, payers have historically excluded coverage for investigational treatments.[59] Insurers typically require data supporting the use of a therapy, and FDA's premarket approval of labeled indications serves as the primary way to satisfy that need.[60]

Currently, thirty-eight states and the District of Columbia have laws or agreements that require private insurers to cover the routine costs of clinical trial participation.[61] Under the Patient Protection and Affordable Care Act of 2010 ("ACA"), private insurers must cover certain trial-related expenses that sponsors do not cover.[62] The ACA requires group health plans or health insurance issuers offering group or individual health insurance coverage to cover routine costs associated with clinical trial participation if the coverage is consistent with what would typically be provided to qualified individuals who are not enrolled in a trial.[63] Under the law,

56. *See* Snyder & Caufield, *infra* note 140. *See generally* Irma Borst et al., *From Friendfunding to Crowdfunding: Relevance of Relationships, Social Media, and Platform Activities to Crowdfunding Performance*, 20 NEW MEDIA & SOC'Y. 1396 (2018).

57. *Id.*

58. *Public or Subsidized Health Insurance*, SMALL BUS. MAJORITY, https://healthcoverageguide.org/reference-guide/coverage-types/public-or-subsidized-health-insurance (last visited May 25, 2020); Amy Fontelle, *Buying Private Health Insurance*, INVESTOPEDIA (Apr. 16, 2020), https://www.investopedia.com/articles/pf/08/private-health-insurance.asp.

59. Won Bok Lee, *Recalibrating "Experimental Treatment Exclusion": An Empirical Analysis*, 83 U. CIN. L. REV. 171, 172–73 (2014).

60. Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 477 (2009).

61. *Insurance Coverage of Clinical Trials*, AM. SOC'Y OF CLINICAL ONCOLOGY, https://www.asco.org/research-guidelines/clinical-trials/insurance-coverage-clinical-trials (last visited May 23, 2020).

62. 42 U.S.C. § 300gg-8 (2018).

63. *Id.*

insurers cannot deny or otherwise alter coverage for a beneficiary that is participating in a clinical trial. Further, the ACA prevents insurers from denying the beneficiary coverage of routine costs for items and services associated with the trial.[64] ACA coverage includes Phase I, II, III, and IV (post-approval) clinical trials conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening diseases, in which death is expected without an interruption in the course of the disease.[65]

D. Medicare

Medicare, the federal health insurance program for people sixty-five and older, younger people with disabilities, and those with end-stage renal disease, began covering the routine costs of qualifying clinical trials in 2000.[66] Medicare considers "routine costs" to comprise all items and services generally available to Medicare beneficiaries that are provided in this context to diagnose, treat, and monitor complications arising from participation in clinical trials.[67] Though Medicare will not cover the costs of investigational items and services themselves, it will cover items and services typically provided to beneficiaries absent participation in a clinical trial that are associated with the provision of the investigational treatment, intended to monitor or prevent complications, or needed for the "necessary and reasonable" care arising from the provision of an investigational treatment.[68]

Medicare does not cover any item or service that would otherwise be statutorily prohibited.[69] For example, Medicare generally does not cover long-term nursing care at home; as such, Medicare would not cover this service for a patient participating in a clinical

64. *Id.*

65. *Id.*

66. *Medicare Program – General Information*, CMS https://www.cms.gov/index.php/Medicare/Medicare-General-Information/MedicareGenInfo/index (last modified Nov. 13, 2019); *Medicare Clinical Trial Policies*, CMS, https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/index?redirect=/ClinicalTrialPolicies (last modified Mar. 27, 2020).

67. *National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1)*, CMS (July 9, 2007), https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=1&ncdver=2&fromdb=true.

68. *Id.*

69. *Id.*

trial.[70] For a clinical trial to qualify for Medicare coverage for participant expenses, the investigational intervention must fall under a Medicare benefit category; the trial must have "therapeutic intent;" and it must enroll patients diagnosed with a disease (i.e., not healthy volunteers).[71] For a clinical trial to qualify for Medicare coverage, the Agency for Healthcare Research and Quality must convene a panel with representatives from multiple Department of Health and Human Services agencies to develop qualifying criteria that will indicate a strong probability that the trial will meet certain desirable characteristics.[72] These characteristics include the extent to which there is available scientific evidence supporting the rationale for the trial and whether the trial's primary goal is to test if the investigational intervention improves health outcomes.[73] Recently, Medicare coverage of clinical trial costs has become more difficult to obtain due to increased standards for analyzing the effectiveness of an investigational intervention.[74]

Though Medicare Part A (hospital coverage) and Part B (medical coverage) pay for a majority of these costs, beneficiaries will likely have to pay some out-of-pocket expenses.[75] Co-insurance for patients is capped at twenty percent of the Medicare-approved amount, and a patient's Part B deductible may apply.[76]

Available data suggests that Medicare expansion of coverage for trial-related expenses significantly increased the number of clinical trial participants ages sixty-five and older, which was an intended effect of the policy change.[77] However, Medicare beneficiaries that also had supplemental insurance were more likely to observe this impact, likely because basic Medicare exposes patients to substantial copayments, even on clinical trial expenses.[78]

70. *Does Medicare Pay for Nursing Homes?*, AARP (2020), https://www.aarp.org/health/medicare-qa-tool/current-long-term-nursing-home-coverage.

71. *See National Coverage Determination (NCD) for Routine Costs in Clinical Trials (310.1)*, *supra* note 67.

72. *Medicare Clinical Trial Policies*, *supra* note 66.

73. *Id.*

74. James D. Chambers et al., *Medicare Is Scrutinizing Evidence More Tightly For National Coverage Determinations*, 34 HEALTH AFF. 253, 253–60 (2015).

75. *Clinical Research Studies*, MEDICARE, https://www.medicare.gov/coverage/clinical-research-studies (last visited May 23, 2020).

76. *Id.*

77. Joseph M. Unger et al., *Impact of the Year 2000 Medicare Policy Change on Older Patient Enrollment to Cancer Clinical Trial*, 24 J. OF CLINICAL ONCOL. 141, 141–44 (2006).

78. *Id.*

E. Medicaid

Unlike Medicare and private insurance, Medicaid is not uniformly required to pay for certain types of trial-related expenses.[79] Rather, Medicaid policies with regard to such expenses are currently left to the discretion of the states.[80] Only ten states and the District of Columbia cover clinical trial participation costs for Medicaid beneficiaries, effectively leaving many Medicaid patients unable to participate in clinical research if at least some costs are not covered by the research sponsor.[81] Congress has looked at this issue, but has not yet passed any legislation. If enacted, the Clinical Treatment Act would guarantee coverage of the routine care costs of clinical trial participation for Medicaid enrollees with a life-threatening condition.[82] There are a large number of medical entities supporting this legislation, including the American Medical Association, the American Cancer Society Cancer Action Network, Friends of Cancer Research, and the American Society of Clinical Oncology.[83]

F. Overall

Despite efforts on the part of many stakeholders to make access to clinical trials more equitable, United States trial participants are likely to be affluent, white, and male.[84] Legal reform is one mechanism of change, yet analyses of state coverage policies have found mixed results on its impact in clinical trial enrollment.[85] An analysis of clinical trial enrollment rates between 1996 and 2001 showed a statistically significant increase in Phase II cancer trial participation, but not in Phase III.[86] Another analysis found little

79. *Health Insurance Coverage of Clinical Trials*, CANCER.NET (Oct. 2018), https://www.cancer.net/research-and-advocacy/clinical-trials/health-insurance-coverage-clinical-trials.

80. *Id.*

81. *See* Chino & Zafar, *supra* note 53.

82. Clinical Treatment Act, H.R. 913, 116th Cong. (2019).

83. *Community Endorsement Letter* (Feb. 15, 2019), https://www.asco.org/sites/new-www.asco.org/files/content-files/blog-release/pdf/2019-clinical-treatment-act-community-support-letter.pdf.

84. Natalie Jacewicz, *Why Are Health Studies So White?*, THE ATLANTIC (Jun. 16, 2016), https://www.theatlantic.com/health/archive/2016/06/why-are-health-studies-so-white/487046.

85. *See generally* Cary P. Gross et al., *Cancer Trial Enrollment After State-Mandated Reimbursement*, 96 J. NAT'L CANCER INST. 1063 (2004).

86. *Id.*

impact of state-mandated insurance coverage on the enrollment of National Cancer Institute Community Clinical Oncology Programs, a mainly non-academic cohort of hospital and oncology practices that aim for community-based recruitment in trials.[87] After the passage of the ACA, insurance coverage for early-phase clinical trials increased for those with private insurance, but there was no change for Medicare or Medicaid insurance holders, who tend to be less affluent.[88] According to another study, insurance denials persisted in cancer clinical trials in recent years, with 62.7 percent of cancer research centers and community-based institutions responding that, at least once in 2014, insurance had been denied to patients seeking clinical trials.[89]

III. EXPANDED ACCESS AND RIGHT TO TRY

If a patient has exhausted all approved treatment options and is not eligible to participate in a clinical trial, there are two other pathways in the United States for use of an investigational medical product: Expanded Access and Right to Try (which are together sometimes called, "non-trial preapproval access").[90] Both mechanisms allow for a patient, through a physician, to request the use of an investigational product from the IND-holder (typically a drug company).[91] To qualify for either pathway, patients must have a serious (under EA) or life-threatening (under EA and RTT) disease or condition and be ineligible to participate in a clinical trial for the product they wish to use.[92] However, there are significant differences between the two pathways in terms of eligibility, oversight, and what type of medical product may be sought.[93] For either

87. Shellie D. Ellis et al., *Effect of State-Mandated Insurance Coverage on Accrual to Community Cancer Clinical Trials,* 33 CONTEMP. CLINICAL TRIALS 933, 933–38 (2012).

88. Kenneth L. Kehl et al., *Insurance Clearance for Early-Phase Oncology Clinical Trials Following the Affordable Care Act*, 23 CLINICAL CANCER RES. 4155, 4161 (2017).

89. Christine B. Mackay et al., *Insurance Denials for Cancer Clinical Trial Participation After the Affordable Care Act Mandate*, 123 CANCER 2893, 2893–95 (2017).

90. Food and Drug Administration, *Expanded Access*, https://www.fda.gov/news-events/public-health-focus/expanded-access; Food and Drug Administration, Right to Try, https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try; s*ee* Carolyn Riley Chapman et al., *Oversight of Right-to-Try and Expanded Access Requests for Off-Trial Access to Investigational Drugs*, 42 IRB: ETHICS & HUM. RES. 2 (2020).

91. *Id.*

92. *Id.*

93. *Id.*

pathway, ancillary and/or direct costs to use experimental products often are the responsibility of the patient.

A. Expanded Access

The FDA's EA pathway, which has existed formally since 1987, allows for single patients or groups of patients to use unapproved investigational treatments outside of clinical trials.[94] Single patients, via their physician, can request the use of an investigational product by identifying a product of interest and making a request to the company or other entity (e.g., academic) developing it.[95] If the IND-holder agrees, the FDA reviews the proposed treatment plan for medical feasibility and a favorable risk/benefit ratio and ensures that the patient is not eligible to participate in a clinical trial.[96] The FDA prioritizes clinical trial participation so that patient usage of investigational medical products may result, through the study, in generalizable knowledge to be used in determining marketing authorization, thereby benefiting future patients.[97] While the agency may alter the proposal, for example, by adjusting dosage or planned safety monitoring, the FDA allows more than ninety-nine percent of these requests to proceed.[98] Except in cases of emergencies, the plan and a consent form must also receive approval by an authorized institutional review board ("IRB") before treatment of the patient.[99]

In addition to accommodating individual patients, the FDA allows sponsors to create cohort expanded access programs, in which a larger number of patients (even up to thousands) may receive an unapproved product.[100] As with the individual patient requests, there needs to be determination that the proposed treatment offers a higher chance of benefit than risk; that there are no

94. *Id.*

95. *Id.*

96. Food and Drug Administration, *supra* note 90.

97. Jonathan P. Jarow et al., *Overview of FDA's Expanded Access Program for Investigational Drugs*, 51 THERAPEUTIC INNOVATION & REG. SCI. 177, 177–78 (2017).

98. Chapman et al., *supra* note 90.

99. Jonathan P. Jarow et al., *Expanded Access of Investigational Drugs: The Experience of the Center of Drug Evaluation and Research Over a 10-Year Period*, 50 THERAPEUTIC INNOVATION & REG. SCI. 705, 705–9 (2016).

100. Kelly McBride Folkers et al., *Patient advocacy organizations' information for patients on pre-approval access to investigational treatments*, 12 BMC RES. NOTES 1, 1–3 (2019).

approved options suitable for these patients; and there is no capability to participate in a clinical trial.[101]

Although patients who receive unapproved medical products via EA are not considered research subjects, and the effort being made on their behalf is considered therapy rather than research, sponsors must collect safety data and report serious or unanticipated adverse events to the FDA.[102] There is increasing interest in collecting efficacy or endpoint data from expanded access, although the value of this endeavor and how to do it without crossing the line into research remain to be sorted.[103] Nevertheless, the hope of generating "real world data" for a product—from a wider population than that enrolled in the product's clinical trials—of interest to regulators or payers may incentivize sponsors to offer expanded access.

Similar to the previously described regulations on charging for investigational medical products under an IND for clinical trials, sponsors that make their products available through the FDA's EA pathway cannot charge patients a profit; charging is limited to the direct costs of manufacturing and shipping the medical product and expenses related to monitoring and collecting safety data. [104] Companies submit these cost calculations to the FDA for review before they can commence charging.[105]

Notwithstanding the legal permissibility of recovering some costs, most biopharmaceutical companies that provide investigational products through EA do so at no cost to the patient.[106] Companies are unlikely to charge for investigational products prior to regulatory approval, to reduce public scrutiny of the market price, which will likely be significantly higher than the direct cost of manufacturing the drug, as revealed by the EA price.[107] Yet even free provision of drugs can also be problematic. After the approval of

101. Jarow et al., *supra* note 99, at 705–6.

102. Elena Fountzilas et al., *Expanded Access to Investigational Drugs: Balancing Patient Safety with Potential Therapeutic Benefits*, 27 EXPERT OP. ON INVESTIGATIONAL DRUGS 155, 155–60 (2018).

103. Kate Rawson, *Expanded Access Data Can Support Approval Decisions, US FDA Says*, PINK SHEET (Nov. 21, 2018), https://pink.pharmaintelligence.informa.com/PS124296/Expanded-Access-Data-Can-Support-Approval-Decisions-US-FDA-Says.

104. GUIDANCE FOR INDUSTRY, *supra* note 36, at 7–8.

105. *See generally id.* at 7–8.

106. Jonathan J. Darrow et al., *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, 372 NEW ENG. J. MED. 279, 281 (Jan. 15, 2015).

107. *Id.*

Firdapse, a drug used to treat a rare neuromuscular disorder, the company set the price at $375,000 annually.[108] Senator Bernie Sanders (I-VT) sent a letter to the company asking for its justification for the price, as the drug had been available to patients for free via EA.[109]

Third-parties may sponsor EA programs. WideTrial, a San Francisco-based company, announced a program last year in which it will sponsor and manage EA programs for treatment use of an agent Oncotelic, Inc. is developing.[110] The FDA approved WideTrial's cost recovery program for a cell-based therapy aimed at treating critical limb ischemia.[111] WideTrial collects data from those who participate in the EA program and sells back this data to the company.[112] The effect on patient costs could be higher, lower, or the same as if the sponsor ran an EA a program itself.

Such recent efforts to find ways for companies to avoid absorbing the cost of providing investigational medical products via EA have developed due to increased awareness of the divide between well-capitalized companies that have money to devote to EA-related expenses and smaller or undercapitalized companies that do not. Pharmaceutical giants such as Novartis and Johnson & Johnson have publicly reported that they fulfill the vast majority of EA requests they receive, and they do not charge for these products in the United States.[113] In contrast, many small companies cite expense as a primary reason for not providing their products via EA.[114] Given this problem, there is renewed interest, among some, in

108. Letter from Bernie Sanders, Senator, U.S. Senate, to Patrick J. McEnany, President and Chief Executive Officer of Catalyst Pharmaceuticals, Inc. (Feb. 4, 2019), https://www.sanders.senate.gov/download/letter-to-catalyst?inline=file.

109. *See generally id.*

110. *WideTrial Partners with Oncotelic to Bring Expanded Access Platform to Cancer*, BIOSPACE (Jun. 3, 2019), https://www.biospace.com/article/widetrial-partners-with-oncotelic-to-bring-expanded-access-platform-to-cancer.

111. Pluristem Therapeutics, Inc., *U.S. FDA Approves Cost Recovery for PLX-PAD under Expanded Access Program in the Treatment of Critical Limb Ischemia,* GLOBENEWSWIRE (Oct. 16, 2018, 7:00 AM), https://www.globenewswire.com/news-release/2018/10/16/1621762/0/en/U-S-FDA-Approves-Cost-Recovery-for-PLX-PAD-under-Expanded-Access-Program-in-the-Treatment-of-Critical-Limb-Ischemia.html.

112. Chris Rauber, *This Man Proposes a Win-Win for Patients and Pharma*, BIZ JOURNALS (May 31, 2018), https://www.bizjournals.com/sanfrancisco/news/2018/05/31/this-man-proposes-a-win-win-for-patients-pharma.html.

113. Steve Usdin, *FDA to Facilitate Access to Unapproved Drugs*, BIOCENTURY (Dec. 14, 2018), https://www.biocentury.com/article/299854/how-fda-plans-to-help-patients-get-expanded-access-to-unapproved-drugs.

114. GUIDANCE FOR INDUSTRY, *supra* note 36, at 4.

having insurance companies cover the costs of investigational products used via EA.[115]

B. Right to Try

Enacted in May 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 sought to streamline access to investigational medical products by eliminating FDA review and IRB approval of single patient requests.[116] The Right to Try Act—which, rather than replacing EA, co-exists with it as another pathway to non-trial access—received significant political support from President Donald Trump and Vice President Mike Pence.[117] The Goldwater Institute, a libertarian organization, developed the concept and first sought to have RTT laws enacted on the state level.[118] Indeed, forty-one states now have their own versions of these laws, creating complexity across jurisdictions to the extent that federal law does not impliedly preempt them.[119]

Several patient groups have expressed frustration that larger numbers of patients have not gained access to investigational treatments through the federal Right to Try Act.[120] Although no centralized authoritative accounting exists as of this writing, it appears that there have been fewer than ten public reports of patients receiving access to an investigational medical product through the federal

115. Peter J. Pitts, *It's Time to Get Serious About the Economics of Expanded Access*, STATNEWS (Jan. 20, 2019), https://www.statnews.com/2019/01/30/get-serious-economics-expanded-access.

116. *See generally* Right to Try Act, Pub. L. No. 115-176, § 204, 132 Stat. 1372 (2018).

117. Angela LaVito, *Trump Signs 'Right-to-Try' Allowing Gravely Ill Patients to Bypass FDA for Experimental Medicines*, CNBC (May 30, 2018), https://www.cnbc.com/2018/05/30/trump-signs-right-to-try-legislation-on-experimental-medicines.html.

118. Zoe Carpenter, *The 'Right-to-Try' Unproven Pharmaceuticals is a Right-Wing Scheme*, THE NATION (Feb. 12, 2018), https://www.thenation.com/article/archive/the-right-to-try-unproven-pharmaceuticals-is-a-right-wing-scheme.

119. Jann Bellamy, *"Right to Try" Laws Create Tremendous Legal Uncertainties; FDA Expanded Access Preferable*, SCI.-BASED MED. (Jan. 17, 2019), https://sciencebasedmedicine.org/right-to-try-laws-create-tremendous-legal-uncertainties-fda-expanded-access-preferable.

120. *See generally* Nicholas Florko, *A Year After Trump Touted 'Right to Try,' Patients Still Aren't Getting Treatment*, STATNEWS (Jan. 29, 2019), https://www.statnews.com/2019/01/29/right-to-try-patients-still-arent-getting-treatment.

Right to Try Act.[121] A number of patients obtained access to one product under the Texas Right to Try Act before the passage of the federal law.[122] In all reported instances to date, it appears the requested product could have been provided under EA, and the rationale for using RTT is unclear.[123]

With regard to costs, the federal RTT statute cites some of the same regulations that apply in the EA context, prohibiting companies from charging more than the direct cost of manufacturing a drug.[124] Yet there are important differences in oversight. The law does not specify who pays for experimental therapies, nor does it specify which entity ensures that these cost calculations are accurate.[125] Thus, patients could bear the costs of paying for the intervention and related costs under RTT. Furthermore, the stated "direct costs" might also be inflated or otherwise adjusted.

Most of the forty-one state RTT laws provide that patients may incur the cost of using an investigational product.[126] However, four state RTT laws have odd and worrisome provisions, which not only allow insurers to exclude coverage for products obtained via RTT, but go further to allow insurers to altogether revoke health insurance coverage for patients undergoing treatment with an experimental therapy.[127] Insurance companies can deny coverage for as long as six months after the experimental treatment ends.[128] These provisions could jeopardize health insurance coverage for those who receive investigational treatments.

121. Mike Riggs, *Trump's 'Right to Try' Law Has Helped at Least Two People So Far. Give Credit Where It's Due.*, REASON (Feb. 5, 2019, 10:35 PM), https://reason.com/2019/02/05/give-credit-where-its-due-at-least-one-p.

122. Zachary Brennan, *Who's Actually Using 'Right-To-Try' Laws? A Texas Oncologist Explains His Experience*, RAPS (Aug. 4, 2017), https://www.raps.org/ regulatory-focus™ /news-articles/2017/8/who-s-actually-using-right-to-try-laws-a-texas-oncologist-explains-his-experience.

123. *See generally* Jen Uscher, *Expanded Access and Right to Try: Alternative Paths to Experimental Treatments for Metastatic Breast Cancer*, BREASTCANCER (2019), https://www.breastcancer.org/symptoms/types/recur_metast/treat_metast/clinical-trials/expanded-access-and-right-to-try.

124. GUIDANCE FOR INDUSTRY, *supra* note 36, at 7–8.

125. Annalisa Merelli, *Who Pays for the "Right to Try" Experimental Medicine?*, QUARTZ (May 30, 2018), https://qz.com/1292947/under-the-right-to-try-act-who-pays-probably-not-insurance.

126. Lisa Kearns & Alison Bateman-House, *Who Stands to Benefit? Right to Try Law Provisions* and *Implications*, 51 THERAPEUTIC INNOVATION & REG. SCI. 170, 171 (2017).

127. *Id.* at 172 (discussing Colorado, Connecticut, Oklahoma, and West Virginia).

128. *Id.*

Currently, there have not been sufficient numbers of patients using the RTT pathway to render a description, much less a prediction, about whether companies tend to charge or not for such access.[129] Shortly after the passage of the federal Right to Try Act, BrainStorm, a company developing a therapy for ALS called NurOwn, announced that it was considering using the federal RTT law to provide access to NurOwn, with cost recovery from patients or other sources.[130] The estimated cost was approximately $300,000 for individual patients.[131] Ultimately, the company decided not to provide NurOwn through RTT, with one exception: Matthew Bellina, a patient who lobbied for the federal RTT law and for whom the bill is named, received NurOwn for free in early 2019.[132]

Finally, there are novel approaches to facilitate funding of EA and RTT access. For example, a new contract research organization called Access Hope (formerly Beacon of Hope) aims to facilitate "Right to Try programs, at scale, for the industry."[133] The company has stated its intentions to provide a stem-cell based product to patients in the future.[134] Access Hope charges individual patients for the cost of an investigational product, while also charging the drug company providing the drug a fee for collecting data from the RTT program.[135] The effect on patient costs could be higher, lower, or the same as if the sponsor handled the RTT request itself. Additionally, proposed model legislation in various states would require any insurers that provide coverage and benefits for palliative care

129. *See* Arthur L. Caplan & Alison Bateman-House, *Should Patients in Need Be Given Access to Experimental Drugs?*, 16 EXPERT OPINION ON PHARMACOTHERAPY 1275, 1276 (2015).

130. Tova Cohen, *Exclusive: BrainStorm Will Not Provide ALS Therapy Under U.S. Right to Try Act*, REUTERS (June 26, 2018, 7:39 AM), https://www.reuters.com/article/us-health-brainstorm-cell-als-exclusive/exclusive-brainstorm-will-not-provide-als-therapy-under-u-s-right-to-try-act-idUSKBN1JM1BE.

131. *Id.*; *see also* Adam Feurstein, *Here Comes the Right-to-try Profiteers. The FDA is Powerless to Stop Them*, STATNEWS (June 20, 2018), https://www.statnews.com/2018/06/20/right-to-try-opportunism.

132. Nicholas Florko, *Prominent "Right to Try" Advocate is Getting Treatment Under the New Law*, STATNEWS (Feb. 5, 2019), https://www.statnews.com/2019/02/05/one-right-to-try-advocate-is-getting-treatment-under-the-new-law.

133. Paul Knoepfler, *Richard Garr Q&A on His New Right-To-Try Firm Beacon of Hope*, THE NICHE: KNOEPFLER LAB STEM CELL BLOG (Sept. 12, 2019), https://ipscell.com/2019/09/richard-garr-qa-on-right-to-try-firm-beacon-of-hope.

134. *Beacon of Hope CRO Launches at ALS Association Florida Chapter's Sixth Annual Hope and Help Symposium*, CISION PRNEWSWIRE (Sept. 12, 2019, 08:29 AM), https://www.prnewswire.com/news-releases/beacon-of-hope-cro-launches-at-als-association-florida-chapters-sixth-annual-hope-and-help-symposium-300917009.html; Knoepfler, *supra* note 133.

135. *Id.*

to provide coverage and benefits for investigational medical products on a basis no less favorable than that of palliative care or hospice.[136] As of this writing, no state legislature has adopted this legislation.

IV. UNREGULATED SALES

For a variety of reasons, including a dissatisfaction with allopathic medicine, a perceived lack of approved treatment options, or willingness to try any option available, very ill patients and their families may wish to access medical interventions marketed and sold outside of, or at the margins of, existing regulatory structures.[137] Such options include alternative medical therapies and modalities, dietary supplements, and homeopathic and/or naturopathic remedies.[138] To access such treatments, patients may resort to "medical tourism," traveling to other locations (sometimes domestic but typically international) to access medical products or procedures that are not locally available to them.[139] Regardless of where access occurs, these interventions are typically unproven; however, only some are "investigational," in terms of being rigorously studied for efficacy and safety.[140] The FDA's lax regulation of all these products means that patients receive injections of various substances that have no proof of safety, efficacy, or even that they contain what they claim.

Stem cell treatments are an important example of this direct-to-consumer phenomenon.[141] Some stem cell treatments are the subject of legitimate clinical trials and medical research.[142] On

136. The Abigail Alliance Patient Advoc. Comm., *The Freedom of Treatment Act: Empowering Terminally-Ill Patients to Try Experimental Drugs and Therapies*, THE ABIGAIL-ALLIANCE (Jan. 21, 2020), https://www.abigail-alliance.org/2020/01/freedom-of-treatment-act-empowering-patients.html.

137. Jeremy Snyder & Timothy Caulfield, *Patients' Crowdfunding Campaigns for Alternative Cancer Treatments*, 20 THE LANCET 28, 28–9 (2019).

138. *See Types of Complementary and Alternative Medicine*, JOHNS HOPKINS MEDICINE, https://www.hopkinsmedicine.org/health/wellness-and-prevention/types-of-complementary-and-alternative-medicine (last visited June 12, 2020).

139. *See generally* I. GLENN COHEN, PATIENTS WITH PASSPORTS: MEDICAL TOURISM, LAW, AND ETHICS (2014).

140. *See generally id.*

141. *See* Geoffrey P. Lomax, Art Torres, & Maria T. Millan, *Regulated, Reliable, and Reputable: Protect Patients with Uniform Standards for Stem Cell Treatments*, 9 STEM CELLS TRANSLATIONAL MED. 547, 547 (2020).

142. *Id.*

the other hand, when heavily marketed as miracle treatments, unproven stem cell treatments can be a potential public health threat.[143] Stem cell treatments can cause a multitude of serious adverse events.[144]

In general, public and private payers do not cover these products or services, which are neither recognized as medically necessary nor supported by an evidentiary basis.[145] Instead, patients seeking to use these options must pay out-of-pocket. Some patients turn to crowdfunding. There is some evidence to suggest that crowdfunding campaigns are not funded equitably, and campaigners with greater perceived social media literacy tend to raise more money on average than those without; additionally, white campaigners tend to raise more money on average than people of color.[146]

GoFundMe is the market leader in personal medical fundraising online, and its website states that it raises more than $650 million for over 250,000 medical campaigns per year.[147] According to GoFundMe's CEO, one in three of the website's campaigns involve medical fundraising.[148] Many of these campaigns involve bona fide medical interventions.[149] For example, in a world of uninsurance and underinsurance, patients and families may raise money to pay large copays in the event of an emergency or to fund long-term care.[150] Accordingly, scholars have found states that did not adopt

143. Laertis Ikonomou et al., *Unproven Stem Cell Treatments for Lung Disease-An Emerging Public Health Problem*, 195 AM. J. RESPIRATORY CRITICAL CARE MED. 13, 13–14 (2017).

144. *See* Amy Zarzeczny et al., *The Stem Cell Market and Policy Options: A Call for Clarity*, 5 J. L. BIOSCIENCE 743, 744–5, 753 (2018).

145. *See* Liz Szabo, *Why Expensive, Unproven Stem Cell Treatments are a New Health Care Trend*, PBS (Apr. 4, 2018, 8:00 AM), https://www.pbs.org/newshour/health/why-expensive-unproven-stem-cell-treatments-are-a-new-health-care-trend.

146. Lauren S. Berliner & Nora J. Kenworthy, *Producing a Worthy Illness: Personal Crowdfunding Amidst Financial Crisis*, 187 SOC. SCI. & MED. 233, 240 (2017).

147. *Get Help With Medical Fundraising*, GOFUNDME, https://www.gofundme.com/start/medical-fundraising (last visited June 12, 2020).

148. Mark Zdechlik, *Go Fund My Doctor Bills: Americans Ask for Help Paying for Health Care*, MPR NEWS (July 2, 2018, 2:00 AM), https://www.mprnews.org/story/2018/07/02/healthcare-gofundme-crowdfunding-doctor-bills-minn.

149. Max Levy, *Bioethics Experts Call on GoFundMe to Ban Unproven Medical Treatments*, THE VERGE (Dec. 9, 2019, 1:51 PM), https://www.theverge.com/2019/12/9/21002593/bioethics-gofundme-health-unproven-medical-treatments-illegal-operations.

150. Mark Zdechlik, *Patients are Turning to GoFundMe to Fill health Insurance Gaps*, NPR (Dec. 27, 2018, 4:29 PM), https://www.npr.org/sections/health-shots/2018/12/27/633979867/patients-are-turning-to-gofundme-to-fill-health-insurance-gaps.

Medicaid expansion after the passage of the ACA held a higher number of crowdfunding campaigns than those that did adopt the expansion.[151]

Frequently, however, people use crowdfunding to raise money for scientifically unsupported and potentially dangerous treatments.[152] Between November 2015 and December 2017, more than one thousand medical crowdfunding campaigns raised more than $6.7 million for a set of five treatments unsupported by scientific evidence: stem cells for brain injury, stem cells for spinal cord injury, homeopathy/naturopathy for cancer, hyperbaric oxygen therapy for brain injury, and long-term usage of antibiotics for Lyme disease.[153] Another study investigating stem cell treatments marketed by 351 United States-based companies found that 408 campaigns raised more than one million dollars for these direct-to-consumer interventions.[154] Unscrupulous health care providers stand to reap significant financial reward from patient use of crowdfunding for treatments that at best are ineffective, and at worst potentially harmful.

V. ETHICAL AND POLICY CONSIDERATIONS

Individuals and families in the United States purchase health insurance so that they can receive financial assistance for medical costs. There is a widespread expectation that insurers will cover the costs of medicines, items, and services that will cure or treat illnesses with the goal of improving one's quality of life.[155] Many Americans, however, find that their expectations surrounding their coverage and what they can afford drastically shift when a patient or loved one becomes gravely ill.[156] In the absence or

151. Berliner & Kenworthy, *supra* note 146, at 237.

152. Ford Vox et al., *Medical Crowdfunding for Scientifically Unsupported or Potentially Dangerous Treatments*, 320 JAMA 1705, 1705-6 (2018); *see also* Jeremy Snyder & Leigh Turner, *Selling Stem Cell 'Treatments' as Research: Prospective Customer Perspectives from Crowdfunding Campaigns*, 13 REGENERATIVE MED. 375, 379 (2018).

153. Vox et al., *supra* note 152, at 1705–6.

154. Jeremy Snyder et al., *Crowdfunding for Unproven Stem Cell-Based Interventions*, 319 JAMA 1935, 1935–6 (2018).

155. Jim Parker, *Biologics and the Principles of Health Insurance*, 9 BIOTECHNOLOGY HEALTHCARE 14, 15 (2012).

156. Lisa McDermott, *How Consumer Expectations Drive Change in Health Organizations*, CERNER (Apr. 13, 2017), https://www.cerner.com/perspectives/consumer-expectations-are-driving-change-in-health-care-organizations.

exhaustion of approved treatment options, seriously or terminally ill patients are sometimes surprised or outraged that an insurer will not cover a last resort investigational product that may provide benefit.[157] We offer both individual-level and population-level bioethics policy analyses.

A. Individualized Bioethics

It is sometimes tempting for an insurer, sponsor, or policymaker—and indeed, the general public—to focus on a particular patient's request for an unapproved treatment rather than focusing on broader policy questions.[158] Scholars refer to this perspective-taking as one of "identified" lives rather than "statistical" lives, and at least psychologically, such framing seems quite important.[159] Such a focus raises serious equity concerns in that objectively similar requests may be treated differently based on how appealing an individual is perceived to be. Petitions for access often underscore factors about the requestor that would invoke sympathy, for example, their age or the fact that they are newly married or a parent.

Access to an unapproved product may be framed as a form of rescue for a desperate person in crisis or danger, like offering a hand to a drowning child in a pond. Through this lens, the moral obligation to help seems almost obvious. Of course, it is limited to situations where there is medical feasibility, no obvious unacceptable risks, and a real chance of benefit to a patient.[160] Such a "rule of rescue"[161] is the basic ethical justification that pharmaceutical and biotechnology companies employ when offering non-trial preapproval access of their investigational products. However, some companies may decline to grant this kind of access using the justification that if they are unable to provide the product to all requestors, then it is unfair to provide it only to some. Alternatively, small companies may not offer this access if doing so would divert resources from

157. *See* Snyder & Turner, *supra* note 152, at 378.

158. I. GLENN COHEN ET AL., IDENTIFIED VERSUS STATISTICAL LIVES: AN INTERDISCIPLINARY PERSPECTIVE 1 (2015), https://www.oxfordscholarship.com/view/10.1093/acprof:oso/9780190217471.001.0001/acprof-9780190217471.

159. *See generally id.*

160. John McKie & Jeff Richardson, *The Rule of Rescue*, 56 SOC. SCI. MED. 2407, 2407–19 (2003).

161. *Id.* at 2407.

clinical trials and cost them the necessary resources to gather data for a regulatory submission.[162]

Such morally salient perspectives can also impinge on companies' rational interests. On the one hand, companies and executives may face costly public shaming if they choose not to provide a product.[163] On the other hand, outside well-defined clinical trials, the clinical risks of providing the investigational product are possibly greater, and adverse outcomes may cause negative publicity or devastating financial losses to the company when those outcomes are disclosed to investors.[164] There is widespread concern within industry that non-trial preapproval access related serious adverse events will hinder the product's progress to FDA approval; however, the FDA has sought to assuage this concern.[165] In a world that depends on drug development by companies, these rational business interests are not irrelevant to public health and ethics.

Even from this individual perspective, there are compelling reasons to constrain coverage for unapproved treatments, aside from the equity concerns raised above. These reasons arise from the principles of non-maleficence and acceptable medical paternalism. Just as insurers or sponsors are in a position to potentially help those in dire need of rescue, they similarly have an obligation to avoid complicity in harming patients who would access dangerous products.[166] Indeed, the duty not to harm, particularly when there is no compensatory benefit, is arguably stronger than the duty to offer a potential benefit. How can sponsors or payers be confident as to whether intervening will do more good than harm, when the majority of investigational medical products ultimately fail?[167]

The typical response to these sorts of concerns is to allow the patient to decide for herself, whether the intervention is likely to be

162. *See generally id.* at 2417.

163. Kenneth I. Moch, *Ethical Crossroads: Expanded Access, Patient Advocacy, and the #SaveJosh Social Media Campaign*, MED. ACCESS @ POINT OF CARE e119, e123 (2017), https://doi.org/10.5301/maapoc.0000019.

164. Goldwater Inst., *Dead on Arrival: Federal "Compassionate Use" Leaves Little Hope for Dying Patients*, RIGHTTOTRY (Feb. 24, 2016), https://righttotry.org/dead-on-arrival.

165. Food and Drug Administration, *Expanded Access | Information for Industry*, https://www.fda.gov/news-events/expanded-access/expanded-access-information-industry#FDAPolicy ("FDA is not aware of instances in which adverse event information from expanded access has prevented FDA from approving a drug.")

166. *Id.* at 1275.

167. Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 1 An Overview of Approval Processes for Drugs*, 1 JACC: BASIC TO TRANSLATIONAL SCI. 170, 171 (2016).

harmful or beneficial on net. However, where reliable information is scant and the choice may be colored by desperation, mere deference to the patient's wishes may be unreliable, for guiding the ethical decisions of others, such as companies and insurers. An analogous concern for clinical trials is the "therapeutic misconception," or the misunderstanding by some research participants that the primary purpose of a clinical trial is to treat them, when it is instead to produce generalizable knowledge.[168]

To the extent that individuals may have a moral right to access some investigational treatments, they also have a right to fair procedures in determining the applicability of that right.[169] The decisions are both drug-focused and patient-focused. At the drug-level, private insurers and government health agencies have relied on technology assessments summarizing the available evidence and gaps in knowledge.[170] If an assessment reveals insufficient evidence on which decisions can be made, insurers will often deny coverage or require additional information.[171] Such assessments consume resources that might be better spent elsewhere.[172] By choosing not to cover investigational therapies as a standard policy, other insurers avoid these situations entirely.[173]

At the individual level, Aetna and Kaiser Permanente have devised a system for external reviews of requests for coverage of investigational therapies by independent medical consultants.[174] In the event that they do not recommend coverage, beneficiaries can appeal those decisions by requesting that a medical ombudsman program, usually a panel of two to three experts who are not affiliated with the insurer, make a clinical assessment of the treatment plan's feasibility for an individual patient.[175] In 1996, California's legislature passed the Friedman-Knowles Experimental Treatment Act, which mandated that all California insurers use a similar

168. Paul S. Appelbaum et al., *The Therapeutic Misconception: Informed Consent in Psychiatric Research*, 5 INT'L J. OF L. AND PSYCHIATRY 319 (1982).

169. *See* Caplan & Bateman-House, *supra* note 129, at 1278.

170. Mary Ader, *Investigational Treatments: Coverage, Controversy, and Consensus*, 5 ANN. HEALTH L. 45, 49 (1996).

171. *Id.*

172. *Id.*

173. *Id.*

174. Norman Daniels & James E. Sabin, *Last Chance Therapies and Managed Care Pluralism, Fair Procedures, and Legitimacy*, 28 HASTINGS CEN. REP. 27, 31–32 (1998).

175. *Id.* at 33.

independent consultation process for reviewing coverage denials.[176] These review processes aim to uphold the principle of procedural justice by ensuring that patients are treated with transparency and fairness when they inquire about or appeal these coverage decisions.

B. Population-Level Bioethics

The foregoing analyses do not answer several population-level questions. Under what, if any, circumstances should coverage for preapproval access be further expanded? How can limits be set fairly and how can access to *unapproved* treatments be rationalized to plan members who are denied reimbursement of certain *approved* medications? Several of these questions impinge on collective action problems.

Although rationing is sometimes considered a dirty word, it is essential in any world of scarce resources.[177] In a world of scarcity, public and private insurers must set reasonable limits on their coverage of items and services to control the costs of health insurance premiums and/or taxes that support coverage in the first place. Allocation of the common pool resource that is health insurance is an important collective action problem, which reflects divergent interests of individuals paying into the pool *ex ante* and individuals drawing from the pool *ex post*.[178]

Given the paucity of evidence about their safety and efficacy, unapproved products are precisely the category of healthcare expenditures that we can be least confident of securing commensurate value for each dollar spent.[179] As frustrating as it may be for a desperate patient to be denied access to an unproven treatment, it is also frustrating for millions of workers to have their real wages depressed for decades as their incomes were instead shifted towards health insurance premiums growing at multiples the rate of inflation.[180] Even worse, if insurance premiums are inflated by spending

176. *Id.* at 34.

177. Nir Eyal et al., *Can Rationing Through Inconvenience Be Ethical?*, 48 HASTINGS CEN. REP. 10, 22 (2018).

178. Einer Elhauge, *Allocating Health Care Morally*, 82 CAL L. REV. 1451, 1459, 1484, 1525 (1994).

179. Christopher T. Robertson, *The Presumption Against Expensive Health Care Consumption*, 49 TULSA L. REV. 627, 636–37 (2014).

180. Darren Lubotsky & Craig A. Olson, *Premium Copayments and the Trade-Off Between Wages and Employer-Provided Health Insurance*, 44 J. HEALTH ECON. 63, 64–67 (2015).

on unproven treatments, some marginal consumers may be unable to get insured at all.[181] Using scarce monies to incentivize preapproval access is problematic when many lack sufficient access to proven basic care. Yet preapproval access to medical problems comes in different forms, some of which it may be more justifiable than others to incentivize. Thus, the question of paying for preapproval access is not a simple yes or no; rather, it is a question of which expenses should be prioritized over which other potential expenditures.

These concerns explain why insurers have traditionally set limits on spending, requiring "medical necessity" and excluding investigational treatments.[182] In routine practice, for approved products to be used on-label, medical necessity primarily entails that a physician identify the treatment as appropriate care for his or her patient, which reflects the teleological purpose of health insurance in the first place.[183] For off-label or investigational treatments recommended by a treating physician, the justification for coverage is more complicated.[184] The product may well prove to be the optimal treatment; the evidence for that claim is just not yet available, or at least has not yet decisively been reviewed by the FDA, which was created for that purpose.[185]

Nonetheless, it is difficult to enforce even reasonable limits. For example, in the 1990s, high-dose chemotherapy followed by autologous bone marrow transplantation ("HDC-ABMT") was a treatment for breast cancer, even though it had a weak evidence base.[186] In response to patient protests and some litigation, many plans agreed to cover the treatment.[187] With the treatment available via insurance, patients desiring it did not have incentive to participate in clinical trials of the intervention, and so the development of

181. E. Richard Brown, *Problems of Health Insurance Coverage and Health Care in the United States: Public and Private Solution Strategies*, 8 CAD. SAÚDE PÚBL., RIO DE JANEIRO 270, 271, 276–78 (1992).

182. Mark A. Hall & Gerald F. Anderson, *Health Insurers' Assessment of Medical Necessity*, 140 PENN. L. REV. 1637, 1645–46 (1992).

183. *Id.* at 1647.

184. *See id.* at 1677, 1682.

185. *See id.* at 1665.

186. Michelle M. Mello & Troyen A. Brennan, *The Controversy Over High-Dose Chemotherapy with Autologous Bone Marrow Transplant for Breast Cancer*, 20 HEALTH AFF. 101, 101–02 (2001).

187. Ader, *supra* note 170, at 50–51, 56.

evidence was delayed.[188] Yet upon completion of these trials, five major randomized clinical trials did not show HDC-ABMT to be effective over standard-dose treatment, and the procedure was ultimately repudiated as ineffective and associated with faster time to death.[189] That episode caused insurance companies to outline clearer policies surrounding coverage of investigational treatments, often limiting them to the confines of clinical trials.[190]

More recently, when courts have addressed such coverage disputes, decisions are often in favor of patients suing for coverage.[191] For example, in 2018, an Oklahoma jury awarded $25.5 million in damages for bad faith insurance denial in a case where a cancer patient sought proton beam therapy, which Aetna determined was investigational or experimental for the patient's specific disease.[192]

Broad insurance coverage of investigational therapies has additional implications for population health. One issue is the collective action problem in the generation of knowledge about safety and efficacy.[193] The generation of knowledge requires investment (typically by companies) in the costs of performing clinical trials, and it requires humans willing to participate in those trials.[194] Accordingly, regulations prohibit companies from profiting from clinical trials, EA, and RTT; such profits would sap their incentive to complete the trials necessary to enter the market broadly.[195] While using scarce monies on unapproved medical products is problematic when many lack sufficient access to proven basic care, such expenditures are justifiable if the investigational products are used in such a way to generate societally-beneficial findings. Insurance coverage for investigational therapies given to patients within the context of a clinical trial ensures a sufficient number of individuals willing to participate in studies that evaluate the safety and effectiveness

188. *Id.* at 50.

189. Mello & Brennan, *supra* note 186, at 102.

190. Ader, *supra* note 170, at 48, 54.

191. *Id.* at 54; Mello & Brennan, *supra* note 186, at 113.

192. Wayne Drash, *Jury Delivers $25.5 million "Statement" to Aetna to Change its Ways*, CNN (Nov. 10, 2018, 4:03 PM), https://www.cnn.com/2018/11/10/health/aetna-verdict-oklahoma-orrana-cunningham/index.html.

193. Robertson, *supra* note 7, at 562, 565.

194. Ahmad W & Moeen Al-Sayed, *Human Subjects in Clinical Trials: Ethical Considerations and Concerns*, 4 J. TRANSLATIONAL SCI. 1, 1–3 (2018).

195. Christopher T. Robertson, *The Tip of the Iceberg: A First Amendment Right to Promote Drugs Off-Label*, 78 OHIO ST. L. J. 1019, 1020 (2017).

of new medical products which could eventually reach the larger patient population. Relatedly, insurance coverage of patient uses of investigational therapies, particularly in the context of clinical trials, can be a form of subsidy for drug innovation.[196] Smaller innovative companies may fail prior to reaching full market approval. If costs can be offset to insurers, or even recouped through revenues, then such companies may be more sustainable.[197] Of course, the challenge becomes picking winners and losers; it is not clear which companies should or should not be subsidized as such.

Even outside of trials, insurers could participate in generating real-world evidence from therapeutic attempts using investigational products.[198] The FDA defines real-world evidence as "clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of [real-world data]."[199] Real-world data is generally considered to be any source of data outside that collected in a traditional, randomized clinical trial.[200] Real world evidence can support label expansions, particularly when the relevant data comes from EA programs, as these may allow sponsors to gather valuable safety and efficacy information about investigational treatments in patients who are different from those in the trial population.[201] Thus, insurers can support innovation while simultaneously participating in generating evidence that aids in their process of determining which products should be added to their formularies. Nonetheless, the collection of real world data from EA runs the risk of blurring the previously sacrosanct division of research and treatment and raising challenges concerning appropriate oversight.

There are also important equity concerns. If an individual insurer, whether it be government-run or private, decides to cover

196. *See* Shailin Thomas & Arthur Caplan, *Incentivizing Therapies for Rare Diseases—Reply*, 322 JAMA 465 (2019).

197. Reed Abelson, *Cost, Not Choice, is Top Concern of Health Insurance Customers*, THE N.Y. TIMES (Aug. 12, 2016), https://www.nytimes.com/2016/08/13/business/cost-not-choice-is-top-concern-of-health-insurance-customers.html.

198. *Real-World Evidence*, U.S. FOOD & DRUG ADMIN. (May 5, 2019), https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence; *Report on Leveraging Real-World Treatment Experience from Expanded Access Protocols*, REAGAN UDALL FDN., https://navigator.reaganudall.org/resources/report-leveraging-real-world-treatment-experience-expanded-access-protocols.

199. *Id.*

200. *See id.*

201. *See id.*

an investigational therapy based on a particular case determination or documented unmet medical need, it must do so in generalizable fashion, treating like cases alike.[202] It should ensure that all patients, regardless of their socioeconomic status, can afford to access this therapy in a clinical trial or through a non-trial pathway. This consideration impinges upon broader social questions of underinsurance, but it is necessary here to recognize the irony of the foregoing ethical rationales for possibly expanding insurance coverage if done in a way that does not guarantee equitable access.[203]

C. Looking Ahead

Given the foregoing ethical and policy concerns, we suggest a few ways forward. The goal is to provide a reasonable degree of access to promising unapproved treatments, with equity and transparency.

The most obvious and pressing opportunity for reform is in the particular context of clinical trials, where the lack of Medicaid coverage for participation costs in many states precludes many low-income patients from accessing potentially beneficial therapies in a clinical trial.[204] Similarly, Medicare should be reformed to place a cap on out-of-pocket expenses for patients in clinical trials (as well as for healthcare more generally). The Medicaid exclusion and uncapped Medicare out-of-pocket exposure not only undermine access but constrict the diversity of clinical trial participants, and thus, the external validity of trial results. This problem has negative ramifications not only for patients who are unable to participate in clinical trials that they would otherwise want to enroll into, but also for society, as new treatments are developed through the clinical trials conducted on such individual volunteers.

Beyond clinical trials, some have suggested changes to Medicaid and Medicare statutes that allow for reimbursement for investigational therapies.[205] Given the challenge of allocating scarce

202. Ader, *supra* note 170, at 51.

203. ROBERTSON, *supra* note 21, at 83.

204. *Guidance for Industry*, *supra* note 36, at 3.

205. Michael Cipriano, *Right to Try Conversation Should be Redirected Toward Reimbursement of Unapproved Drugs, Experts Say*, PINK SHEET (Jan. 29, 2019), https://pink.pharmaintelligence.informa.com/PS124659/Right-To-Try-Conversation-Should-Be-Redirected-Toward-Reimbursement-Of-Unapproved-Drugs-Experts-Say.

resources, this approach presents extremely difficult line-drawing problems.

A more modest approach would be to create new federal tax subsidies to companies, perhaps targeting smaller biotechnology companies in particular, to support their capability to create EA programs where they believe the evidence and medical need justify such. This approach avoids the two perils of allowing broad insurance coverage of unproven treatments and allowing companies to profit from unapproved treatments. This approach facilitates the creation of EA programs while keeping companies focused on proving safety and efficacy for broad market access, when insurance reimbursement would be appropriate.

There has also been a suggestion that sponsors develop early-stage conversations with payers so that reimbursement is "preapproved."[206] Others have suggested allowing companies to profit from preapproval sales, but then placing the profits in interest-bearing escrow accounts.[207] If the drug is not approved as safe and effective for the patient's indication, then insurers can claw back the profits.[208] If it is approved, they are released.[209] One such mechanism under Congressional consideration is the Conditional Approval Act, which would create a new pathway to FDA approval, similar to the current accelerated approval pathway.[210] Conditional approval would be provisional and would be automatically revoked if follow-up trials supplying sufficient proof of safety and efficacy are not conducted within a set time period.[211] As companies would be able to sell their conditionally-approved medical product for a profit, they would have an incentive to make it widely available, unlike with clinical trials or non-trial preapproval access.[212] As an approved product, public and private payers could choose to cover the product's costs, something they are very unlikely to do for products

206. Pitts, *supra* note 115.

207. Benjamin P. Falit & Cary P. Gross, *Access to Experimental Drugs for Terminally Ill Patients*, 300 JAMA 2793, 2794 (2008).

208. *Id.*

209. *Id.*

210. S. 3133, 116th Cong. (2019).

211. *Id.*

212. *See generally Advancing the Development of Medical Products Used in the Prevention, Diagnosis, And Treatment of Neglected Tropical Diseases: Hearing before the FDA*, 111th Cong. (2010) (statement of Leonard Sacks, Acting Director, Office of Critical Path Programs).

provided via non-trial preapproval access.[213] However, simply because payers could choose to pay does not mean that they necessarily would do so. A further complication is that the company would be obliged to continue clinical trials of the product, yet its commercial availability could negatively impact enrollment.[214] Such post-approval trials have already proven difficult for companies to complete.[215]

VI. CONCLUSION

Disparities in access may result when costs for access to investigational medical products fall solely, or even largely, on individuals. Ultimately, public and private insurers are justified in setting limits on coverage for investigational products. Using scarce monies on unapproved medical products of unknown worth is problematic when many lack sufficient access to proven basic care and inflated premiums cause other welfare tradeoffs. However, it is laudable to try to offer rescue in cases of last resort, particularly when this can be accomplished in ways that generate societally-useful data, e.g., clinical trials and real world evidence-generating expanded access programs.

Thus, Congress should consider mechanisms that encourage the pharmaceutical and biotechnology industry to cover the costs associated with clinical trials, including extending Medicaid and Medicare coverage of non-investigational product costs ancillary to preapproval access. Secondarily, non-trial pathways may warrant additional support, but these reforms must keep in mind the fundamental roles and incentives of innovating companies to prove safety and efficacy and of insurers to limit coverage to interventions with proven value. Finally, such reforms must be carried out in ways that avoid negative impacts on patient access to approved treatments or other evidence-based medical interventions.

213. *Working Group on Compassionate Use & Preapproval Access Frequently Asked Questions*, NYU LANGONE HEALTH, https://med.nyu.edu/departments-institutes/population-health/divisions-sections-centers/medical-ethics/research/working-group-compassionate-use-preapproval-access/frequently-asked-questions#who-pays-for-preapproval-access-drugs (last visited May 31, 2020).

214. S. 3133.

215. Steven Woloshin et al., *The Fate of FDA Postapproval Studies*, 377 NEW ENG. J. MED. 1114 (2017).