



TRIALS AND TRIBULATIONS:

How to Remove Barriers Blocking Cancer Patients From Clinical Trials and Advance the Next Generation of Treatment



LEUKEMIA &
LYMPHOMA
SOCIETY®

PAGE

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About The Leukemia & Lymphoma Society:

This report was commissioned by The Leukemia & Lymphoma Society® (LLS). LLS is a global leader in the fight against cancer. The LLS mission: Cure leukemia, lymphoma, Hodgkin's disease, and myeloma, and improve the quality of life of patients and their families. LLS funds lifesaving blood cancer research around the world, provides free information and support services, and is the voice for all blood cancer patients seeking access to quality, affordable, coordinated care. To learn more, visit www.LLS.org. For more information on this report, please contact phil.waters@lls.org.

The Manatt logo consists of the word "manatt" in a lowercase, white, sans-serif font, centered within a solid yellow rectangular box.

About Manatt Health:

This analysis and report was prepared by Julian Polaris, Alex Morin, and Donna O'Brien of Manatt Health. Manatt Health is an interdisciplinary policy and business advisory division of Manatt, Phelps & Phillips, LLP, one of the nation's premier law and consulting firms. Manatt Health helps clients develop and implement strategies to address their greatest challenges, improve performance, and position themselves for long-term sustainability and growth. For more information, visit www.manatt.com/health.

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EXECUTIVE SUMMARY

Clinical trials are a lifesaving option for many cancer patients. But too many patients face barriers preventing access to this critical treatment.

Everyone suffers when patients cannot access clinical trials. Today's patients miss out on potentially lifesaving treatments, and future patients may not gain access to newer, potentially better treatments as quickly as they could have, otherwise.

This report identifies major coverage-related barriers that too often block eligible blood cancer patients from clinical trials—and offers a menu of policy remedies. Notably, many of these findings also apply to patients with other cancers.

These findings are based on interviews with a broad group of stakeholders nationwide, including health providers operating cancer clinical trials; payers that offer commercial, Medicare Advantage, and Medicaid managed care plans in different states; and blood cancer patients with firsthand experience of pursuing or participating in trials.

Those stakeholders identified several major problems standing between patients and trials:

- **Confusion about coverage requirements.** Some payers misunderstand federal requirements to cover routine patient costs associated with clinical trials. That confusion can lead to delays in enrollment and financial hardship for patients.
- **Unnecessarily complex administrative processes.** Enrolling in and completing a clinical trial can be complicated and time-consuming—at a time when patients' health may depend on beginning treatment quickly.
- **Lack of access to out-of-network trials.** For many patients, the best trial option involves providers outside their insurer's network. Commercial plans typically do not cover out-of-network providers, making participation difficult and expensive for potential participants.
- **Unique challenges for patients with Medicaid coverage.** These patients, who have lower incomes, face ongoing barriers to trial enrollment despite new federal laws.

The study offers the following recommendations to solve these problems:

- **Amend coverage requirements for routine patient costs associated with clinical trials.** Exempting routine care from cost-sharing, and requiring coverage for out-of-network trials, would reduce the financial burden on patients.
- **Require trial sponsors to protect insured trial participants from out-of-pocket costs.** This would ensure that patients do not have to pay for essential services required for the trial.
- **Streamline processes for prior authorizations and single-case agreements.** Patients and providers alike would benefit from this step that could reduce delays and administrative hassles.
- **Strengthen provider networks to include providers that offer blood cancer clinical trials.** With more options available to patients, they will have an easier time finding both convenient and affordable trials.

- **Ensure the Clinical Treatment Act can be as effective as possible for those with Medicaid coverage.** The law requiring Medicaid coverage of routine trial costs took effect in 2022. It can be strengthened with new federal guidance for providers and a more streamlined approach to prior authorization.

Together, these policies represent a significant step forward in making clinical trials more accessible to patients. Notably, these solutions provide policymakers with an opportunity to advance health equity, as trial enrollment often reflects the same disparities that persist throughout our healthcare system.

These steps can improve patients' ability to participate in clinical trials, contribute to research, and receive the best possible care. In many cases, these recommendations will improve efficiency for doctors and insurers as well. Through these policies, clinical trials can work better for everyone involved.



01 BACKGROUND

Ensuring Timely Access to Clinical Trials Saves Lives Today and—by Advancing Science—Saves Lives Tomorrow

People living with blood cancer today have a better chance of survival than ever before, thanks to stunning scientific progress in recent decades. For certain blood cancers, survival rates have more than doubled over the last 50 years.¹ To gain full advantage of these advances, however, blood cancer patients often need timely access to highly specialized care, including clinical trials.

For some patients, clinical trials offer the most promising treatment for their condition or access to new treatments with reduced or more manageable side effects.² This situation is especially true for trials studying investigational drugs and procedures that represent the future of blood cancer treatment, but are not yet widely available across all sites of care.

In addition to the benefits for trial participants, improving access to clinical trials will reap benefits for future blood cancer patients as well. The faster clinical trials complete enrollment, the faster they can generate research findings that advance the field for the benefit of future patients, potentially paving the way for the development of a new drug or establishing the benefits of an experimental procedure.³

With the rise in “precision” oncology—in which treatments are tailored to patients or cancers with specific genetic profiles—some clinical trials are designed for ever-smaller cohorts of patients with specific characteristics, reducing

the number of potentially eligible patients and, therefore, increasing the importance of ensuring access for patients who are both clinically eligible and interested in participating.

Simultaneously, clinical trial enrollment must reflect the clinical and demographic characteristics of the patients who will ultimately use the product or procedure under investigation. Currently, clinical trial enrollment too often reflects the same disparities evident in other aspects of healthcare access and outcomes, including significant disparities along lines of race, socioeconomic status, and other demographic factors.

In 2020, for example, among clinical trials supporting applications for Food and Drug Administration (FDA) approval of new drugs and biologics, only 8% of participants were Black (whereas 14% of Americans overall are Black), and 11% were Hispanic or Latino (compared to 19% of Americans overall); this mirrors the persistent racial disparities in cancer care and cancer mortality.^{4,5} The reasons for these disparities in clinical trial enrollment are many and complex—including factors regarding lack of referrals for clinical trials, exclusionary clinical eligibility criteria, and ability to access clinical trials—and, while researchers and policymakers have launched initiatives going back over three decades, progress has been modest at best.⁶

Under Federal Law, Most Health Insurance Includes Coverage of “Routine Patient Costs” Associated with Blood Cancer Clinical Trials

In clinical trials, the trial sponsor may cover certain services. For example, when a pharmaceutical manufacturer is studying an investigational drug that has not yet received FDA approval, the manufacturer will typically not charge trial participants or their insurance for the drug itself—indeed, federal law prohibits them from doing so except in certain circumstances.ⁱ However, trial sponsors typically do *not* cover the cost of other services necessary for the trial protocol, but are consistent with the standard of care. For these services—which may include diagnostic imaging, laboratory tests, physician office visits, inpatient hospital services, and so on—the healthcare providers bill the patient’s insurance. If any services are not covered by the patient’s insurance, the patient must pay for those out-of-pocket costs consistent with the hospital’s financial assistance policy, unless the provider elects to absorb those costs.

Historically, some healthcare payers used to deny coverage for all services associated with clinical trials on the grounds that such services were, by definition, “experimental.” This created a barrier to clinical trial participation, especially for lower-income patients who could not afford the potentially significant out-of-pocket costs. This situation contributed to the disparities in access to clinical trials and the lack of diversity in clinical trial enrollment, as noted above. However, as a result of federal policy changes over the last 25 years, all major payers are now generally prohibited from denying coverage for so-called “routine patient costs” associated with qualifying clinical trials, meaning that if a service is furnished in accordance with the payer’s standard coverage rules for clinical care, the payer cannot deny coverage solely on the basis that the service happens to be performed in connection with a clinical trial.ⁱⁱ

i For additional guidance, see FDA. Charging for Investigational Drugs Under an IND—Questions and Answers: Guidance for Industry. June 2016. <https://www.fda.gov/media/85682/download>. FDA has proposed, but not yet finalized, updates to this guidance document, as shown here: <https://www.regulations.gov/document/FDA-2013-D-0447-0009>.

ii The definition of a “qualifying clinical trial” varies by payer, but generally includes blood cancer trials conducted with federal funding or under federal oversight (e.g., in connection with an application for FDA approval of a new drug).

Federal Coverage Requirements for Routine Patient Costs Associated with Clinical Trials

- Since 2000, this requirement has applied to the **Medicare program**,⁸ a federally administered program covering people over the age of 64 and people with certain disabilities.
- A similar coverage requirement has applied to **commercial plans**—including employer-sponsored plans and Marketplace plans—since the Affordable Care Act went into effect.⁹
- Congress extended this policy to the **Medicaid program**—a joint federal-state program that covers low- and middle-income people—only as of January 2022, pursuant to the Clinical Treatment Act¹⁰ (although some states had voluntarily adopted a policy of covering at least some routine patient costs under clinical trials¹¹).

This policy has a few important limitations:

- Payers are **not required to cover the investigational item or service being studied** in the trial if it does not satisfy standard coverage rules, such as investigational drugs not yet approved by the FDA.ⁱⁱⁱ However, payers *are* responsible for any items or services *necessary for the administration* of the investigational product. For example, in a blood cancer clinical trial studying chimeric antigen receptor (CAR) T-cell therapy, the trial sponsor may cover the cost of the manufacturing of the CAR-T product itself, but the patients' payers may be required to cover chemotherapy and other services necessary to administer the CAR-T therapy.

- Payers are generally **not required to cover monitoring activities performed solely for purposes of the clinical trial**—i.e., monitoring activities exceeding the standard of care. However, disagreements occasionally arise about whether a given imaging test, blood draw, or other diagnostic or monitoring service is consistent with the standard of care. If the trial sponsor believes that a particular service is a “routine patient cost” that insurance should cover, the sponsor generally will not offer to cover those costs under the clinical trial budget. However, if a trial participant’s insurer then declines coverage on the grounds that the service is not medically necessary, those costs could potentially fall on the patient unless the provider absorbs them under its standard financial assistance policy or as part of a trial-specific financial assistance policy. To protect the integrity of the research and confirm the effectiveness of investigational treatment, conducting monitoring in a standardized way across all trial participants is important. Thus, if a patient faces out-of-pocket costs for certain services and is unable or unwilling to pay, the patient may not be permitted to participate in the trial at all.

iii The trial sponsor will typically bear those costs, as noted above.

- **Commercial plans are not required to cover services related to an out-of-network clinical trial** if the plan does not normally cover out-of-network services. Some plans include an out-of-network benefit (typically with higher cost-sharing), while other plans exclude coverage for out-of-network services; these latter plans are not currently required to cover routine patient costs for out-of-network clinical trials.^{iv}

- **Patients remain responsible for any cost-sharing** that would normally apply to routine patient costs under the trial. That responsibility includes any differences in the cost-sharing that may apply for in- vs. out-of-network services.

To illustrate these principles, consider the coverage implications of the following hypothetical trial protocol:

Service Required Under Trial Protocol	Expected Insurance Coverage Under “Routine Patient Costs” Policy
A CT scan consistent with the standard of care	Likely covered by the patient’s insurance, with standard cost-sharing*
An investigational chemotherapy drug not yet approved by FDA	Likely <i>not</i> covered. However, the trial sponsor typically covers investigational drugs.
The service of administering the investigational chemotherapy drug in an infusion center	Likely covered by the patient’s insurance, with standard cost-sharing*
Blood draws and laboratory tests to monitor the patient’s condition, consistent with the standard of care	Likely covered by the patient’s insurance, with standard cost-sharing*
Additional blood draws and laboratory tests that go beyond the standard of care but are required under the clinical trial protocol to gather necessary data regarding the safety and efficacy of the investigational chemotherapy	Likely <i>not</i> covered. The trial sponsor will typically cover such costs, although sometimes payers have unanticipated disagreements about the standard of care. In such circumstances, if a payer refuses to cover a service, the provider must decide whether to absorb that cost or pass it on to the patient.
Services to diagnose and treat complications arising from the investigational product, consistent with the standard of care	Likely covered by the patient’s insurance, with standard cost-sharing*

* If a commercial plan does not cover out-of-network services, the plan is not required to cover routine patient costs for an out-of-network clinical trial. By contrast, enrollees in Medicare Advantage and Medicaid managed care are entitled to coverage of routine patient costs for clinical trials regardless of whether the provider is in their plans’ network or located in their home state.

iv By contrast, for enrollees in Medicare Advantage plans and Medicaid managed care organizations (MCOs)—privately administered plans that contract with the federal or state governments to deliver Medicare or Medicaid benefits, respectively—federal law guarantees coverage of routine patient costs regardless of whether the furnishing provider is in or out of network for the patient’s health plan, and regardless of whether that provider is located in the patient’s home state. Additionally, for Medicare Advantage enrollees, routine patient costs are billed to the Medicare fee-for-service system rather than the Medicare Advantage plan.

PATIENT PERSPECTIVE

The Patels' Story:

When High-Quality Coverage Still Isn't Enough

For years, Nila Patel managed the relationship her husband's medical practice had with insurance companies, so she had a pretty good handle on how medical coverage works. But when their son Rajan was 9, he was diagnosed with a rare B-cell acute lymphoid leukemia—and Nila's expertise wasn't enough. "I thought I could handle any prior authorization or appeal we needed," she said. "But that wasn't what happened."

Rajan went through standard treatment and seemed to be doing well, but the family knew more care might be needed in the future. That's why they invested in high-quality insurance, a Platinum plan, via her husband's business. When enrolling, Nila even double checked that they would be able to use the plan outside of the Patels' home state of Maryland and was told it would be covered. The premiums for the Platinum coverage would be more expensive, but given Rajan's cancer, she knew it could be worth it.

After multiple rounds of treatment, including a round of CAR T-cell therapy, Rajan unfortunately relapsed again in April 2022. The Maryland hospital where he'd received most of his treatment couldn't provide him access to the clinical trial services he needed. The Patels needed to travel to Pennsylvania to the closest children's hospital with the right kind of trial. That's when Nila learned that the plan wouldn't cover out-of-state care unless it was an "emergency."

"I spent hours on the phone, trying to get the right prior authorizations and ensure that everything would be covered, only to learn that beyond the trial, nothing else would be covered," she said. "If something went wrong, we'd be on the hook for any additional care my son needed, or treatment could be delayed." In other words, if Rajan got treatment at home in Maryland, they'd be covered. But the treatment he needed wasn't available in his state.

After months of exhausting uncertainty and countless hours on the phone, Nila bought a new healthcare plan, and this time, asked much more detailed questions about any emergency exclusions for out-of-state care. Unfortunately, this delay meant they missed the window during which they needed to enroll in the trial. Finally, in September—nearly 6 months after he initially needed the treatment—Rajan was able to join the clinical trial in Pennsylvania and receive a second round of CAR-T.

While the Patels have now reached over a year of remission from this successful treatment, they don't want anyone to go through what they had to go through. "I had so much expertise, I had the flexibility at work to spend hours on the phone on hold, and I asked all the right questions," Nila said. "But even that wasn't enough."

For Many Patients, Cost and Coverage Concerns Are a Barrier to Clinical Trial Participation

Despite the federal coverage guarantees described above, LLS continues to hear from patients who have insurance but encounter barriers when seeking to participate in clinical trials. Indeed, research has indicated that fewer than 10% of all adult cancer patients participate in a clinical trial—a figure that reflects multiple “structural and clinical hurdles that stand in the way of trial participation for most patients,” according to a recent meta-analysis in the *Journal of the National Cancer Institute (NCI)*.¹² There are threshold hurdles, for example, related to finding a trial matching their specific disease (which can be a challenging and labor-intensive process, especially for individuals whose treatment provider is not actively involved in clinical trials^v), as well as the need to be screened for the clinical eligibility criteria for the trial (which can exclude many patients due to factors such as age, disease stage, or comorbidities).

Once a patient clears all those hurdles, coverage issues should not be a barrier to participation. However, the research shows that among patients who decline to participate in a trial despite eligibility, a commonly reported barrier was concerns about out-of-pocket costs.¹³ This finding is consistent with the conversations of LLS with patients who call its Clinical Trial Support Center, a free service connecting patients with nurse

navigators assisting them through the clinical trial process. (<https://www.lls.org/support-resources/clinical-trial-support-center-ctsc>).

Some patients are denied coverage by their health plan for services necessary for participation in the trial but not covered by the trial sponsor, which often means they are ineligible to participate unless they themselves pay for those services out of their own pocket. As discussed above, this may include monitoring or other services that the trial sponsor believed to be consistent with the standard of care, but which do not align with the coverage policies of a particular payer. This scenario can also present for a patient with a commercial plan not covering out-of-network services.

Even for patients approved for coverage by their health plan, barriers may be related to coverage-related processes—such as prior authorization or rate negotiations between plans and providers—which delay the initiation of trial services by weeks or even months. Typically, for a cancer patient, time is of the essence as their disease continues to progress.

^v The evidence shows that participation rates in clinical trials can vary significantly across treatment settings. At research hospitals designated as “Cancer Centers” by NCI, nearly 20% of adult patients participate in clinical trials, whereas at community cancer centers—where the majority of cancer patients are treated—the trial participation rate is much lower at 4%. See: [Nationally representative estimates of the participation of cancer patients in clinical research studies according to the commission on cancer](#). | *Journal of Clinical Oncology*.



Study Methodology

To better understand these processes and barriers, interviews were conducted with stakeholders representing providers from multiple states that offer robust cancer clinical trial programs—including academic medical centers, specialized cancer hospitals, community hospitals, and safety-net hospitals—as well as health plans offering Medicare Advantage plans, Medicaid MCOs, and commercial plans across multiple states. The following section outlines the findings from

these interviews and the author’s critical review of the granular steps needed to determine coverage and potential out-of-pocket costs for a cancer patient found eligible for a clinical trial, including consideration of the special challenges associated with out-of-network access. Each is paired with actionable strategies for providers, payers, and policymakers to mitigate the coverage-related barriers to clinical trial access for blood cancer patients.

02 FINDINGS AND RECOMMENDATIONS

Finding #1

Payers and Providers Agree on the Value of Clinical Trial Participation for Cancer Patients In Most Cases

All stakeholders agreed that clinical trials can provide valuable treatment opportunities for participants and generate valuable knowledge for cancer researchers, as described above, and also that there are opportunities to improve on the current coverage processes for clinical trials.

Stakeholders emphasized, in addition, key benefits that can accrue to health plans when their members enroll in clinical trials:

- When a trial studies an investigational drug or other item, the trial sponsor typically bears the associated costs, as noted above. Thus, although the payer may be billed for routine patient costs, the payer is not financially responsible for a central—and potentially costly—component of the treatment regimen. For example, a recent study found that Medicare spent an average of \$6,000 less on chemotherapy and other drugs for cancer patients enrolled in clinical trials as compared to unenrolled patients.¹⁴
- For enrollees in Medicare Advantage, traditional Medicare covers routine patient costs associated with clinical trials. Thus, the enrollee’s Medicare Advantage plan is not financially responsible for those services, except in the following circumstances:
 - If the Medicare Advantage plan provides lower cost-sharing than traditional Medicare does, the plan will be responsible for covering the difference between those cost-sharing amounts for routine patient costs associated with the trial.
 - Although unlikely, if the treatment provider and the Medicare Advantage plan negotiate a reimbursement above traditional Medicare rates for routine patient costs under the trial, the plan must pay the difference.

Some provider trial sites reported, however, that they occasionally encounter resistance regarding coverage for routine patient costs associated with clinical trials. Providers are required to identify which services related to a clinical trial are to be billed to the patient or their insurance, but in some cases, payer staff may make their own inquiries based on the patterns observed in a provider's billing (perhaps facilitated by claim analysis algorithms). Payer staff may deny a prior authorization outright or may hold payment pending further investigations. At best, this delays payment to the provider, and at worst, can result in multiple rounds of follow-up that consume staff time for both payer and provider.

This resistance may, in some instances, reflect a misunderstanding about the federal requirement for coverage of routine patient costs, particularly for staff originally trained on older policies concerning exclusions for clinical trial coverage. This dynamic may also reflect a misunderstanding by the payer staff about the scope of services typically covered by the trial sponsor. Understandably, payers seek to ensure that they are not being billed for services whose costs were already covered, but as noted above, trial sponsors typically expect that providers will bill the patient's insurance for services consistent with the standard of care and not within the negotiated trial budget. The burden falls on providers to ensure that they do not improperly bill for already covered services and they face potentially severe penalties if they knowingly violate this policy, especially with respect to services billed to the public Medicare or Medicaid programs.

PROMOTE AWARENESS OF CLINICAL TRIAL COVERAGE AND ACCESS REQUIREMENTS:

STRATEGIES FOR ALL STAKEHOLDERS

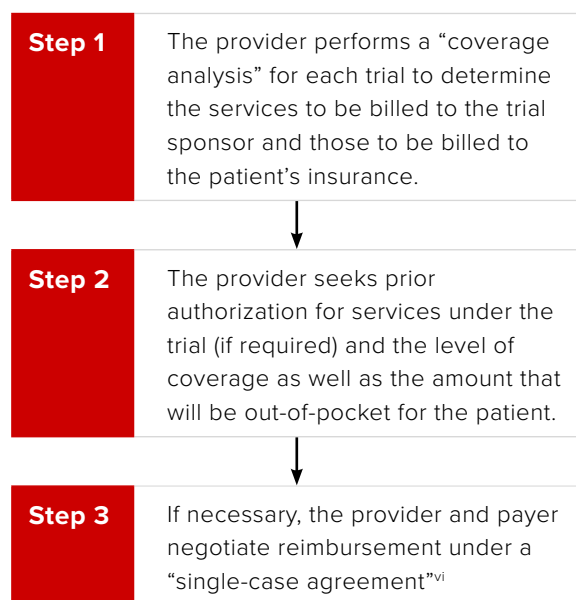
1.1. Elevate awareness of federal and state requirements for clinical trial coverage among stakeholders involved in supporting patient clinical trial enrollment and ensure that payer and provider staff are appropriately trained in clinical trial enrollment processes.

Payers and providers have a responsibility to continuously train and inform staff navigating coverage and payment for clinical trials on current federal (and applicable) state law and streamline requirements on each side to the extent possible to successfully enroll and cover patients in a timely fashion. Tools from federal policymakers to make requirements as clear as possible will facilitate the closure of any knowledge gaps.

Finding #2

Administrative Processes to Enroll and Successfully Complete Clinical Trials Can be Significantly Streamlined through Provider, Payer, and Policymaker Action

Three key steps are needed to determine coverage and expected out-of-pocket costs associated with a patient’s participation in a clinical trial once they identify a trial and are deemed clinically eligible:



Each step represents precious time for patients whose lives may be on the line and providers, payers, and policymakers each have an opportunity—and a responsibility—to streamline each.

STEP 1 THE PROVIDER PERFORMS A “COVERAGE ANALYSIS” AND ESTIMATES EACH PATIENT’S OUT-OF-POCKET COSTS

For each clinical trial, a provider must analyze coverage to identify the specific services the trial sponsor will cover, as well as the routine patient costs (i.e., services consistent with the standard of care) that should be billed to the trial participant’s insurance. This coverage analysis typically involves coordination between the provider’s billing department and the clinical and research staff conducting the clinical trial. Some providers develop a template coverage analysis at the outset of the trial to expedite the process of assessing coverage for each individual participant later on, potentially including consideration of services not required for all patients under the trial protocol, but that may be necessary for specific patients to manage symptoms, diagnose and treat complications, or address suboptimal treatment response.

vi Typically required only for out-of-network providers serving enrollees in commercial or Medicaid managed care plans.



For each individual deemed clinically eligible for a trial, the provider must then assess coverage under the patient's insurance and estimate the patient's out-of-pocket expenditures (if any) associated with the trial, including any required cost-sharing for covered services as well as consideration of services that will likely not be covered. This estimate, typically conducted and communicated to the patient through the provider's patient financial services staff, will be revised as needed as the provider confirms the scope of coverage and reimbursement through the steps below.

If there are any services that are required for participation in the trial, but that are not covered by either the trial sponsor or the patient's insurance, the provider may pass those costs onto patients subject to the provider's standard policy on patient financial assistance or may opt to absorb specific trial-related costs across *all* trial participants to bolster trial recruitment and retention.

For patients facing significant estimated out-of-pocket costs, providers may require an upfront deposit for the patient to proceed with the trial. Depending on the provider and the patient, this deposit may be in the thousands, the tens of thousands, or the hundreds of thousands of dollars—an amount many patients are unable to pay. Providers report that large out-of-pocket estimates are associated with factors such as the following:

- Patients whose health coverage includes significant co-insurance or a high deductible, as standard cost-sharing rules apply to the coverage of routine patient costs associated with clinical trials.
- Patients who seek access to an out-of-network trial, but who are enrolled in a commercial plan with no coverage or highly restricted coverage for out-of-network services, trial-related or otherwise.^{vii}
- The trial sponsor incorrectly predicting which services would be covered as routine patient costs or a physician determining that an additional test is needed above the standard of care but not on the trial budget. This situation occurs most often with repeat monitoring services such as diagnostic imaging or laboratory tests, with payers denying coverage based on their policies about the maximum frequency for such services or an ad hoc determination of medical necessity.^{viii}

Steps can be taken to better protect patients against the out-of-pocket costs to participate in a clinical trial.

vii Unlike Medicare Advantage plans and Medicaid MCOs, commercial plans are not required to cover the routine patient costs associated with out-of-network trials to a greater degree than they cover out-of-network services in general, as discussed above

viii As discussed above, the requirement for coverage of routine patient costs generally requires payers to cover the same services they would normally cover outside a clinical trial, so a payer may, for example, seek to apply its standard frequency limitations to trial-related services.

PROTECT AGAINST OUT-OF-POCKET COSTS FOR PATIENTS IN CLINICAL TRIALS

STRATEGIES FOR FEDERAL POLICYMAKERS

2.1. Congress should amend the coverage requirement for “routine patient costs” associated with clinical trials, across all federally regulated payers, to reduce financial burdens on patients seeking trials both in and out of network.^{ix}

Specifically, Congress could do the following:

- a. Exempt routine patient costs from cost-sharing requirements, such as deductibles or coinsurance, regardless of whether similar services would normally be subject to cost-sharing outside of a clinical trial;
- b. Require commercial plans to cover routine patient costs in out-of-network clinical trials, regardless of whether the plan typically covers out-of-network services (thereby aligning with the existing policies for Medicare Advantage and Medicaid managed care); and/or
- c. Require coverage for monitoring activities or variations on the standard of care, which do not involve unapproved drugs or devices, regardless of whether such services are consistent with the payer’s standard coverage outside clinical trials (similar to the coverage rule for services “necessary for the administration” of the investigational item or service being studied). Such services are necessary for participation—and have been deemed essential for monitoring treatment safety and efficacy—in a clinical trial

conducted with federal funding or otherwise pursuant to federal oversight.

2.2. Require, as a condition on federal research grant funding for blood cancer trials, that trial sponsors protect insured trial participants from out-of-pocket costs, whether by covering such costs under the trial budget or by securing agreement from all participating providers to absorb any such costs.

STRATEGIES FOR STATE POLICYMAKERS

2.3. State policymakers should adopt similar coverage requirements for routine patient costs associated with the clinical trials in insurance markets they regulate, including Marketplace plans and in Medicaid Managed Care.

STRATEGIES FOR PROVIDERS/TRIAL SITES

2.4. Ensure that trial budgets include funds to pay for all services required under the trial protocol, which payers are likely to view as inconsistent with the standard of care.

2.5. Implement operational improvements for clinical trials teams (scientific and administrative/financial) to eliminate unnecessary delays and errors in enrolling patients in trials and implement financial assistance policies that promote streamlined trial enrollment. Specifically, providers could do the following:

- a. When undertaking a new clinical trial, promoting upfront coordination between the provider’s clinical and finance teams to develop a

^{ix} State legislators could establish similar policies for state-regulated insurers as well as their state Medicaid programs.

trial-specific template with a clear identification of costs borne by the trial sponsor, and those likely billable to the patient insurance as a “routine patient cost,” and those which do not fall into either of these categories.

- b. Developing enhanced financial assistance policies for trial participants to ensure that inadequate coverage or disputes over the standard of care do not present barriers to clinical trial participation.

STRATEGIES FOR PAYERS

- 2.6. **Commercial payers should review their policies and, if necessary, add coverage for out-of-network clinical trials for cancer patients, regardless of whether the plan otherwise covers out-of-network services.**

STEP 2 THE PROVIDER SEEKS PRIOR AUTHORIZATION FOR SERVICES UNDER THE TRIAL

For specialized cancer services—trial-related or otherwise—payers often require the provider to seek prior authorization, meaning that the provider must confirm coverage *before* providing those services to be eligible for payment. Additionally, health plans with provider networks typically require prior authorization for any services performed by out-of-network providers, and state Medicaid programs often require prior authorization for any services by out-of-state providers.

The prior authorization process can take a few days or up to a week for many therapies and services, with some new therapies such as CAR-T taking even longer. Requests for out-of-network access typically take longer than requests by a provider in the plan’s network. Some plans contract with third-party vendors to process prior authorization requests. Providers report that some vendors have more experience with cancer care than others. Lack of vendor expertise can delay prior authorization processes.

With respect to the Medicaid program, federal law requires prior authorization decisions within 72 hours for trial-related services, as noted above. Additionally, CMS has proposed—but not yet finalized, as of the time of writing—regulatory reforms that would streamline and standardize prior authorization procedures across all federally regulated payers.¹⁵

Some payers have higher average denial rates than others do concerning prior authorization requests. If a payer denies prior authorization, the patient can appeal and present arguments about why this service qualifies for coverage under the payer’s policies and governing law. However, the appeal process can be complex, cumbersome, and lengthy, as LLS has explored in prior reports with specific policy recommendations for federal and state policymakers.¹⁶

STRATEGIES TO PROMOTE TRIAL ACCESS: STREAMLINE THE PROCESS FOR PRIOR AUTHORIZATIONS

STRATEGIES FOR FEDERAL POLICYMAKERS

- 2.7. Federal policymakers should strengthen and finalize their proposals to streamline and digitize prior authorization across federally regulated payers.^x**

STRATEGIES FOR STATE POLICYMAKERS

- 2.8. State policymakers should align all state-regulated markets with federal proposals to streamline and digitize prior authorization.**

STRATEGIES FOR PROVIDERS

- 2.9. Standardize templates used by clinical trial staff to streamline prior authorization and eliminate unnecessary delays due to process errors.**
- 2.10. Negotiate broader language in prior authorizations to allow for latitude for additional tests and other services based on physician judgment to avoid having to re-negotiate every change.**
- Because it is difficult to predict all the tests and treatments a cancer patient will need when undergoing treatment or on a clinical trial and with unanticipated complications, some providers aim for a broader language in the prior authorizations to allow for latitude for additional tests and other services, based on physician judgement to avoid having to re-negotiate every change. This strategy avoids further delays and saves the time of payer and provider staff.

STRATEGIES FOR PAYERS

- 2.11. Ensure appropriate education and training for staff and third-party vendors on clinical trials.**
- Appropriate education and training for payer staff and third-party vendors can help to avoid unnecessary delays or coverage denials due to misunderstandings about the coverage dynamics described above, including the legal standard for coverage of routine patient costs under clinical trials.

^x LLS has submitted comments on this regulation.

STEP 3 IF NECESSARY, THE PROVIDER AND PAYER NEGOTIATE REIMBURSEMENT UNDER A “SINGLE-CASE AGREEMENT”

A “single-case agreement” refers to an agreement between a payer and a provider regarding the reimbursement for a specific set of services furnished to a specific patient—i.e., a “single case.” If the provider is in the payer’s network, a single-case agreement is not typically needed because the necessary reimbursement details are already defined in the existing network-provider agreement. For out-of-network providers, a single-case agreement is generally required to define which services will be covered (building on the prior authorizations in Step 2), and at what rate. Specialized providers who attract a significant number of out-of-state and out-of-network patients may negotiate several hundred single-case agreements every year (including clinical care unrelated to clinical trials as well as trial-related routine patient costs).

Single-case agreements typically take more than a week to negotiate and can sometimes take multiple weeks. Factors that can extend these negotiations include the following:

- Disagreements between the provider and the payer about the appropriate scope of services to include under the agreement. For example,
 - The payer may assert that in-network providers could perform certain services under the trial protocol, such as imaging scans or laboratory tests. Shifting these services in-network may help to reduce the overall costs of care for the payer.
 - Providers, however, may prefer that all services connected with the clinical trial be performed onsite to ensure that services are performed consistently across trial participants and that all monitoring results are obtained in a timely manner.

Additionally, providers have noted the potential burden on patients if they must make multiple visits to multiple provider sites for trial-related services, particularly if those sites are far apart.

- Disagreements between the provider and the payer about the appropriate reimbursement rate for these services, which are more likely to arise if the services in question are relatively new and do not yet have widely known and widely accepted prices or rate methodologies.
- Administrative complexity. Some payers have dedicated staff who focus on single-case agreements for out-of-network providers, who may be separate from the teams that oversee prior authorization. Providers report that sometimes, they have difficulty identifying the appropriate person to contact about specific issues concerning out-of-network care, and may need to repeat information as they proceed through conversations with the separate teams handling prior authorization and single-case agreements.

While these negotiations are ongoing, some providers are comfortable moving forward with trial enrollment and the initiation of services, as long as they have a prior authorization in hand. Other providers, however, have a policy of not starting services until the completion of both prior authorization *and* a single-case agreement, noting that in some cases, the provider and payer are unable to agree on a single-case agreement at all.

Additionally, providers expressed frustration about the narrow parameters for certain single-case agreements, with the result that any change in the patient’s plan of care may require the agreement to be “reopened” for negotiations, which can generate additional administrative burdens for staff and potential delays in patient care.

STREAMLINE THE PROCESS FOR SINGLE-CASE AGREEMENTS

STRATEGIES FOR FEDERAL POLICYMAKERS

2.12. Implement policies to avoid the need for, or minimize the delays associated with, single-case agreements for clinical trial participation.

Today, a single-case agreement is necessary only when the provider and payer must negotiate rates, typically when (1) the patient is enrolled in a commercial plan or Medicaid managed care plan, and (2) the provider is outside the payer's provider network. (For Medicare Advantage enrollees, routine patient costs associated with clinical trials are reimbursed under Medicare fee-for-service, as noted above.) Potential strategies could include, for example, the following:

- a. For states with Medicaid managed care programs, the state could "carve out" routine patient costs for clinical trials from the managed care contract and reimburse for such services through the fee-for-service delivery system. This carve-out could be applied specifically to out-of-network trial-related services, or (as in Medicare) could apply to trial-related services across the board.
- b. To minimize the delays associated with single-case agreements, policymakers could establish rate parameters for commercial plans and Medicaid managed care organizations concerning out-of-network clinical trials, such as a requirement that reimbursement for such services may be no less than the current rates are under Medicare fee-for-service. If an

out-of-network provider is willing to accept that default rate, the single-case agreement would be much more straightforward to negotiate, or could potentially be bypassed entirely, depending on the circumstances.

STRATEGIES FOR STATE POLICYMAKERS

2.13. States can similarly implement policies through their regulatory power to eliminate the need for, or minimize delays associated with single-case agreements for clinical trial participation including requirements in Medicaid and Medicaid managed care and through state-regulated commercial plans.

STRATEGIES FOR PROVIDERS

2.14. Standardize templates used by clinical trial staff to streamline single-case agreements.

2.15. Negotiate broader language in single-case agreements to allow for latitude for additional tests and other services based on physician judgement to avoid having to re-negotiate every change.

- a. If these services are not addressed in the initial single-case agreement, the agreement may need to be reopened to incorporate these services, resulting in further administrative burden and potential treatment delays.

Finding #3

Patients Often Must Seek Clinical Trials Out-of-Network as Their Only Option, Which Presents Greater Coverage and Access Challenges

Patients, providers, and payers all agreed that clinical trial coverage dynamics are more complex, and potentially more burdensome, when a provider conducts the trial outside the health plan’s provider network.

Even outside the context of clinical trials, cancer patients often encounter access barriers related to narrow provider networks and challenging processes for securing out-of-network access, potentially including the need to appeal an initial denial of service authorization, as LLS has discussed at length in prior reports.¹⁷ Complex clinical trials are typically conducted by institutions—including academic medical centers and standalone cancer hospitals—that NCI has designated as “Cancer Centers” for their leadership in “state-of-the-art research focused on developing new and better approaches to preventing, diagnosing, and treating cancer.”¹⁸ As a result, blood cancer patients are especially likely to need access to clinical trials outside the provider network of their plan and/or across greater geographical distances, including across state lines.

Indeed, prior studies have found that, even when patients live in a state that is home to one or more NCI-Designated Cancer Centers, those providers are often excluded from their health plan’s provider network.¹⁹ During the interviews, an NCI-Designated Cancer Center reported that among patients enrolled in its clinical trials, approximately four out of five were referred to the clinical trial after beginning treatment with another provider, including many patients who travel from out of state.

Through direct plan action or federal/state policy action, provider networks could be strengthened to ensure in-network access to these kinds of facilities and providers. In prior LLS reports, different strategies have been outlined, including the following:^{xi}

- Increasing oversight of reporting about provider networks using enhanced data sources such as all-payer claims databases to better understand the construct of provider networks and the availability of certain services;
- Requiring plans in different insurance categories to contract with NCI-designated cancer centers and other types of specialty cancer providers where trials are most often found;
- Strengthening coverage standards for second opinions and access to treatments out-of-network based on second-opinion recommendations.

xi For additional recommendations regarding network adequacy standards, see LLS’s recent report, *Vital Access: How Policymakers Can Streamline the Cancer Care Journey*, available from https://www.lls.org/sites/default/files/2023-01/vital_access_2023.pdf.

PROMOTE TRIAL ACCESS THROUGH PROVIDER NETWORK REQUIREMENTS

STRATEGIES FOR PAYERS AND FEDERAL/STATE POLICYMAKERS

3.1. Strengthen provider networks to include providers that offer blood cancer clinical trials. Patients would benefit if their plan’s provider networks includes the leading cancer care providers in their state or region. By enhancing in-network access to NCI-Designated Cancer Centers and other leading providers of cancer clinical trials, this approach would help to avoid the delays and administrative burdens associated with out-of-network access. Payers can voluntarily act to strengthen their networks, and federal and state policymakers should consider reforms to the network adequacy standards across payers to promote access to clinical trials and other essential blood cancer services.

Travel Costs Can Be a Significant Barrier to Clinical Trial Participation

Although this study focused on coverage-related issues for services under clinical trials, stakeholders were also unanimous in noting the unique access challenges for patients who must travel long distances to access clinical trials. These observations are consistent with the research finding that “having to travel to participate in a trial can be an overwhelming burden to patients.”²⁰ A patient who lives in a rural region of the state may need to drive several hours for each visit to a specialized facility in an urban center. Some patients may be unable to participate in a distant clinical trial absent financial assistance with transportation, local room and board, child care, and other needs. The Medicaid program and certain other health plans may offer limited coverage for such supports, but coverage tends to be fairly modest, where it exists at all.

The overall lack of support for these travel-related needs likely contributes to a lack of diversity in clinical trials by, for example, suppressing participation of people who have lower incomes, who have young children (especially single parents), or who live in rural areas. Congress is considering—and LLS supports—legislative solutions to reduce these financial and logistical barriers to clinical trial access and otherwise support the enrollment of diverse patient populations.^{xii}

xii See, for example, the NIH Clinical Trial Diversity Act of 2022 (S.5268/H.R.7845), <https://www.congress.gov/bill/117th-congress/senate-bill/5268/>.

Finding #4

The Medicaid Program Presents Special Challenges for Enrolling in and Completing Clinical Trials

The Medicaid program must be part of any strategy to improve clinical trial diversity, given that Medicaid enrollees are, by definition, lower income, and are also disproportionately likely to be racial minorities, or to live in rural regions.^{21,22} Currently, however, the Medicaid program presents coverage-related issues beyond those that apply across all federally regulated payers.

Ongoing Implementation of the Clinical Treatment Act.

As noted above, only in January 2022 did federal law begin requiring state Medicaid programs to begin covering routine patient costs associated with qualifying clinical trials pursuant to the Clinical Treatment Act, including for providers outside the patient’s provider network or home state. Additionally, this law established two key procedural protections:

- Prior authorization for routine patient costs associated with clinical trials must be decided within 72 hours
- Prior authorization must be completed based on a standardized attestation form^{xiii} developed by the federal government, in which the principal investigator and (if different) the treatment provider of the trial list the National Clinical Trial Number (from the federal registry at [ClinicalTrials.gov](https://clinicaltrials.gov)) and sign a certification that the trial is “appropriate” for the patient. States and MCOs are not permitted to request any additional information about the clinical trial to approve coverage.

Although this law has now been in effect for over a year, stakeholders report that implementation is still a work in progress. For example, providers have expressed uncertainty about the role of the attestation form, which, in their view, appears to burden them to assess whether a given clinical trial service qualifies for coverage under the policy. Providers have also noted the lack of understanding regarding the definition of a “qualifying clinical trial” under this policy, which is limited to trials that (among other criteria) address a “serious or life-threatening disease or condition.” Although this term is defined in certain FDA policies regarding oversight of drugs and medical devices, providers have expressed a need for clarifying guidance about whether they should apply that same definition in the context of Medicaid coverage.

Providers have noted, as well, that some states have introduced additional steps in the prior authorization process beyond those required by federal law, such as a requirement for the attestation form to be reviewed and approved by both the MCO and a state official, which adds time to the prior authorization process. New York is an example of this.

xiii The standardized attestation form is available here: <https://www.medicaid.gov/resources-for-states/downloads/medicaid-attest-form.docx>.

SUPPORT IMPLEMENTATION OF THE CLINICAL TREATMENT ACT

STRATEGIES FOR FEDERAL POLICYMAKERS

4.1. CMS should issue additional guidance to ensure that providers and trial sites clearly understand the Clinical Treatment Act.

In particular, providers would benefit from additional guidance about how to use the standardized attestation form, what documentation providers should maintain to demonstrate compliance, and the definition of a “qualifying clinical trial.”

STRATEGIES FOR STATE POLICYMAKERS

4.2. States should consider opportunities to streamline prior authorization processes required under the Clinical Treatment Act, including avoiding duplicative review of the standardized attestation form.

4.3. States should continue to monitor compliance with the CTA requirements and issue provider bulletins and other tools to continue to educate stakeholders and promote trial enrollment in the Medicaid population.

Provider Enrollment. An additional issue specific to the Medicaid program concerns provider enrollment. Generally, state Medicaid programs are required to screen and enroll all providers before they may bill for services. Although states are permitted to waive or relax these requirements for certain out-of-state providers—including providers already screened and enrolled in the Medicaid program of another state and/or providers offering services to a managed care enrollee pursuant to a single-case agreement—relatively few states have taken up these options. Although the Clinical Treatment Act requires states to provide coverage for out-of-state clinical trials, it does not require states to streamline the provider enrollment processes that are a condition for payment.

Hence, a highly specialized provider that attracts patients from all over the country may need to enroll in dozens of state Medicaid programs to receive payment for services. In addition to the administrative burdens associated with researching the requirements of each state, filling out the required forms, and gathering the necessary supporting documentation, the approval process takes time to complete, and states generally require providers to complete the enrollment process *before* they begin offering services. At best, this delays the start of clinical trial services and treatment for patients traveling across state lines. At worst, it can deter providers from serving patients from states with particularly burdensome enrollment requirements.



STREAMLINE MEDICAID ENROLLMENT FOR OUT-OF-STATE PROVIDERS

STRATEGIES FOR STATE POLICYMAKERS

4.4. For an out-of-state provider already enrolled in Medicare or its home state Medicaid program, States should exercise their flexibility under the existing law to streamline enrollment. Specifically, states could take the following steps:

- a. Offer expedited screening and enrollment processes; and/or
- b. Allow retroactive enrollment, so that the provider may begin treatment while the enrollment process is underway.
- c. States could implement these reforms specifically for an out-of-state provider offering a clinical trial or could extend these policies to out-of-state providers more generally.

STRATEGIES FOR FEDERAL POLICYMAKERS

4.5. To ensure that provider enrollment does not present a barrier to clinical trial access, Congress or CMS could consider *requiring* states to implement these flexibilities, at least concerning a provider that seeks authorization for out-of-state clinical-trial-related services under the CTA.

03 CONCLUSION

Clinical trials are a potentially lifesaving option for many blood cancer patients, and they are also the path to developing new cancer treatments, yet access to trials continues to be a major challenge for many patients. Despite federal coverage guarantees for routine patient costs associated with qualifying clinical trials, too many patients continue to run up against coverage-related barriers, including coverage denials or delays associated with coverage processes such as prior authorization and single-case agreements. These barriers are particularly acute when, as is all too common, the right trial for a cancer patient is outside the provider network of their plans, and potentially outside their home state.

Implementing the strategies outlined in this report, healthcare stakeholders can help remove coverage-related impediments to cancer patients' participation in clinical trials, in addition to streamlining administrative processes for providers and payers alike and advancing research on the cancer cures of tomorrow.

Endnotes

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