EXECUTIVE INSIGHTS

Unlocking Clinical Trial Success: Strategic Coverage of Patient Care

In a world where weak patient recruitment is the leading reason most clinical trials run behind schedule, only 2%-5% of U.S. patients currently participate in trials.[1] Patients are the core of any clinical trial; without them, there would be no progress in the development of novel therapies or innovation in care. As such, a key focus of clinical trial sponsors is ensuring patient participation in and completion of clinical trials. There has been significant research in understanding barriers to clinical trial participation. However, much of this research has been focused on understanding methods of improving access to clinical trials (e.g., expanding access within community populations) or the indirect expenses associated with participation (e.g., travel and lodging).

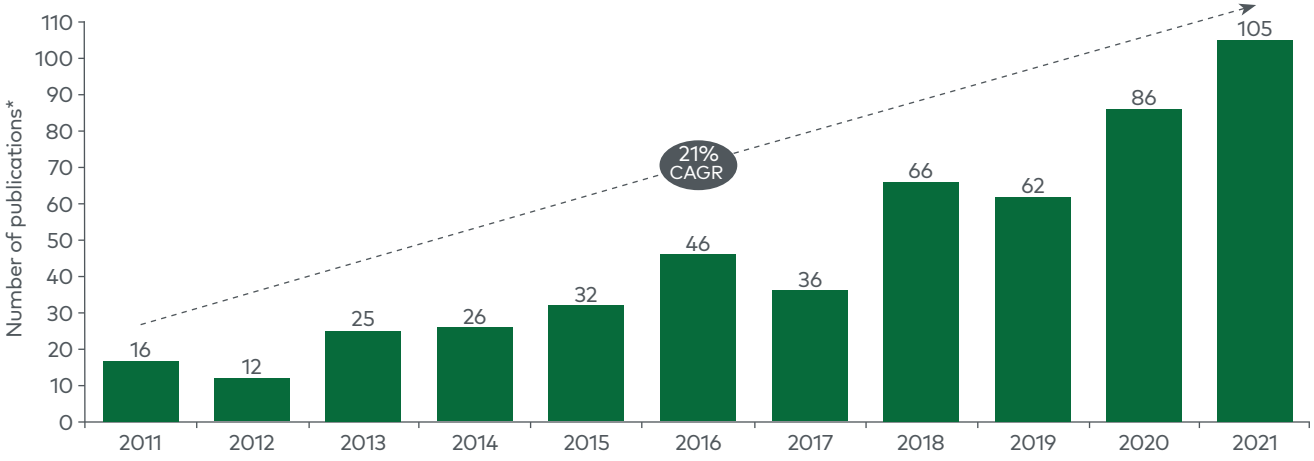
While lack of adequate support may be a contributing factor in lack of participation, another factor may be hindering both participation and driving patient drop-out in the U.S.: coverage of care of baseline or comparator drugs (i.e., standard of care therapies), which in other countries, such as the U.K., are borne by the sponsor.[2] This factor may especially impact diverse patient populations that are more socio-economically vulnerable.

The current state of care coverage in cancer trials

While coverage of care has improved over the past two decades through the Affordable Care Act[3] and through individual state legislation,[4] there are still significant holes in coverage. Insurance plans are not obligated to cover a clinical trial conducted outside the plan's provider network, including pharmacy/medical drug benefit designs, which can include drug exclusions even if a therapy is standard of care. Plans established prior to March 23, 2010,

are not required to change benefit structures to cover costs associated with clinical trials. Additionally, if care in the clinical trial involves an off-label use of therapy, ambiguity may exist, and coverage may lapse. The combination of all these factors has resulted in a growing concern among both sponsors and patient advocates about "financial toxicity." Over the past 10 years, studies related to this term have increased globally (see Figure 1). Furthermore, patient surveys show that financial-related concerns are often the most cited, with 16%-47% of patients who are actively receiving treatment reporting a high financial burden.[5]

Figure 1
Publications over time on "financial toxicity" in academic literature



*Number of publications on "financial toxicity" in breast cancer patients
Note: CAGR=compound annual growth rate
Source: Cheng et al., Medicine (Baltimore), 2023

The lack of or lapses in insurance coverage negatively impact sponsors, resulting in lower participation rates in trials and therefore slower timelines for therapy development. Due to this, questions naturally arise: Should sponsors consider covering baseline or comparator drugs in clinical trials to help drive clinical trial participation, and are there benefits to sponsors for doing so?

Improved coverage for patients has aggregate benefits for sponsors, hospitals, caretakers and the patients themselves. Sponsors can improve trial efficiency by removing insurance approval/processing hurdles and can help drive access to therapies that have potential to save patients' lives. Additionally, sponsors can improve timelines for innovative therapies by increasing the speed of trial recruitment by removing financial barriers to participation. Hospitals and caretakers can take part in cutting-edge research while also providing quality care for patients who are looking for novel, innovative therapies. Patients enrolled in trials can receive care and remain in those trials, with fewer concerns and burdens related to participation, while moving research forward for those who come after them.

Developing a framework to understand sponsor coverage impact

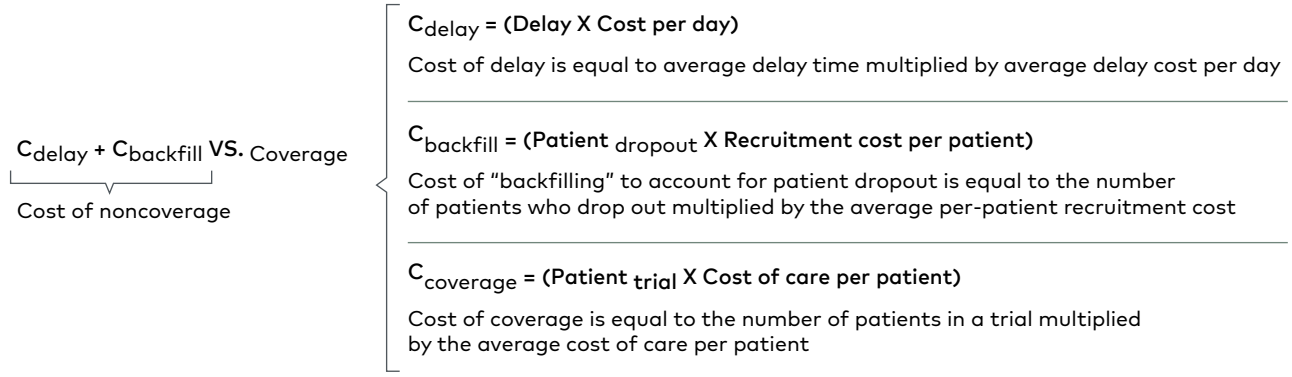
If a clinical trial sponsor were to cover the cost of therapy for a clinical trial participant, would that outweigh the costs it faces if it does not? Additionally, are there other "soft" benefits to ensuring coverage of care for trial participants? To answer this, we looked to understand the key costs/factors affecting clinical trials. We suggest sponsors should evaluate covering the cost of therapy from a total-cost-of-trial perspective rather than just the immediate economics of drug cost itself. This evaluation should be comprehensive, including factors such as diversity (especially given recent Food and Drug Administration guidance).

Costs related to trial operations are often fixed, while those related to patients are often variable. Less apparent costs include those related to clinical trial delays. Often trial delays are related to patient recruitment delays and/or patient dropout because of financial burden, lack of therapy efficacy or adverse events. Some studies indicate that delaying a clinical trial by only one day can result in up to $8 million in lost drug revenue.[6]

If a sponsor were to consider coverage of baseline therapy, it would need to factor in the cost of baseline therapy coverage on a per-patient basis as a variable cost. Providing coverage would eliminate any variable costs associated with patient dropout such as patient recruitment or trial delays. However, if a sponsor does not provide coverage of baseline therapy, it risks completing a trial with a lower number of patients and continuation with a less robust dataset.

Based on the above, we developed a framework based on known costs (excluding fixed costs) to a clinical trial sponsor. We have summarized this framework in an equation that weighs the cost to a sponsor for noncoverage of baseline therapy versus the cost of coverage of care (see Figure 2).

Figure 2
Key costs associated with coverage of baseline therapy and noncoverage



Source: L.E.K. research and analysis

The cost of noncoverage can be broken into two main parts: the cost associated with the delay of a clinical trial and the cost associated with "backfilling" or recruiting for patients who dropped out during the trial. On the other hand, the cost of coverage is simply the cost of covering care (i.e., standard of care therapy) for a trial participant.

Cost of noncoverage versus cost of coverage

To illustrate the framework more clearly, we have outlined conservative, moderate and aggressive examples of an early-stage oncology trial based on 100 trial participants (see Figure 3). Across both coverage and noncoverage of baseline therapy, we account for patient dropout and associated costs.

In the moderate example scenario where a sponsor does not provide coverage of baseline therapy, we can see that to begin a clinical trial with 100 patients, the sponsor must start with a much larger pool of screened and qualified patients, to account for patients who decline to participate. After the trial begins, around 9% of participants will drop out for financial reasons, with additional dropout for nonfinancial reasons. Ultimately, the trial will have 75 patients who are eligible and complete the trial, but it will require backfilling of 25 patients. Considering the cost of backfilling and the delays associated with this, the total cost to the sponsor of noncoverage is about $64 million.

If the sponsor were to provide coverage of baseline therapy, it would reduce the number of patients declining to participate for financial reasons to zero, expanding the number of patients who begin the clinical trial to 148. Additionally, over the course of the trial, no patients would drop out for financial reasons, resulting in 124 patients who would be eligible and could complete the trial. This could allow the sponsor to further screen those patients and ensure that 100 patients complete the trial. However, we must account for the per-patient cost of baseline therapy for the clinical trial; assuming that all patients receive baseline therapy and only require coverage of out-of-pocket expenses, the cost would be approximately $7 million.

If we compare the cost of coverage versus noncoverage, the apparent cost savings is roughly $57 million. The bulk of these savings stems from eliminating the delays that a clinical trial would experience, ultimately affecting the sponsor's time to launch. Using more conservative or aggressive assumptions, adjusting the amount of out-of-pocket cost a patient may face, and using the logic laid out previously, the sponsor may be able to drive cost savings ranging from about $16 million to about $144 million.

It is important to note that this is an illustrative example that makes various assumptions regarding size of trial, delays in timeline, lost revenue and cost of baseline therapy. There is a point at which a trial size may become too large, the cost of coverage of baseline therapy may be too prohibitive or the projected revenue of the therapy in development is not as large. However, there are cases in which sponsor coverage of baseline therapy will be worthwhile due to projected savings. At the outset of any trial planning processes, sponsors should assess the overall cost/benefit analysis and explore all potential options available to drive better outcomes.

Figure 3

Illustrative analysis comparing cost of coverage of baseline therapy versus cost of noncoverage

	Number of patients (with no coverage of care)	Number of patients (with coverage of care)	Assumptions: Cost of noncoverage	Conservative	Moderate	Aggressive
Screened and qualified patients	**238**	**238**	C_{delay} = (30 days^^ X cost per day)	~$18M^^^	~$60M^*	~$150M††
Decline to participate for **financial reasons***	**(48)**	—	$C_{backfill}$ = (25 patients X cost per patient)	~$930K*^	~$4M^^*	~$75M†††
Decline to participate for **other reasons****	**(90)**	**(90)**				
	100	**148**	$C_{noncoverage}$ = C_{delay} + $C_{backfill}$	~$19M	~$64M	~$157M
Drop out for **financial reasons*****	**(9)**	—				
Drop out for **other reasons^**	**(16)**	**(24)**	**Cost of coverage** $Patient_{trial}$ = 100 X cost of care per patient = $C_{coverage}$	~$3M**^	~$7M†	~$13M†*
Eligible and complete clinical trial	**75**	**100**				
	(Will require backfilling of 25 patients)	(Results in surplus of 24 patients, which can be whittled down to the full 100)	**Cost savings = Cost of noncoverage – cost of coverage**	**~$16M**	**~$57M**	**~$144M**

*Assumes 58% of patients decline to participate, with 35% of 58% (i.e., ~20%) stemming from financial reasons regarding coverage of care
**Remaining ~38% of patients who decline for nonfinancial reasons
***Assumes 25% dropout rate, with 35% of 25% (i.e., ~9%) stemming from financial reasons regarding coverage of care
^Remaining 16% of patients who drop out for nonfinancial reasons
^^Estimate of 30 days based on statistic that 94% of clinical trials experience delays longer than one month
^^^Conservative estimate of $600K in potential revenue lost per day
*^Utilized $37,050 per-patient recruitment cost for phase 1 trial
**^Assumed average cost of novel oral medication is $135K coupled with coinsurance of 25%
^*Moderate estimate of $2M in potential revenue lost per day
^^*Utilized $175K per-patient recruitment cost for phase 1 trial
†Assumed average cost of novel oral medication is $135K coupled with coinsurance of 50%
††Aggressive estimate of $5M in potential revenue lost per day
†††Utilized $300K per-patient recruitment cost for phase 1 trial
†*Assumed average cost of novel oral medication is $135K coupled with no coverage by insurer
Source: Strategic Patient Screening Q&A," Clinical Performance Partners (2014); Chino and Zafar, American Society of Clinical Oncology Educational Book (2019); Advarra; Bell et al., British Medical Journal (2013); Alexander, Pharmacy and Therapeutics (2013); Avantor; Chaudhari et al., Perspectives in Clinical Research (2020); CenterWatch; Sertkaya et al., Clinical Trials (2016); Health Cost Institute and Dusetzina SB, The Journal of the American Medical Association Oncology (2016); American Society of Clinical Oncology (ASCO); Employer Health Benefits Survey, Kaiser Family Foundation (2022)

A case for coverage

As shown, for an early-stage oncology trial, there is clear potential for cost savings for sponsors that elect to cover the cost of care for trial participants. In addition to the financial benefits, there are other benefits such as improving trial participation and reducing dropout (e.g., only 90 patients declining to participate versus 138).

Recruiting for clinical trials may also improve as screened and qualified patients who previously may have dropped out for financial concerns or access barriers related to baseline or standard of care therapy would be more likely to be retained as their care would be covered fully with no significant out-of-pocket expenses or surprise costs. As financial barriers are removed and the pool of patients increases, sponsors may be able to reduce the number of trial sites, further increasing cost savings (site costs, excluding personnel, have been estimated to range from about $400,000 to roughly $3 million[7]). Furthermore, there are "soft" or intangible benefits of covering cost of care, including improvement of sponsor perception as a "sponsor of choice"; supporting access to care among a broader, more diverse group of patients; enabling patients to help move therapy innovation forward for those to come; and improving timelines for therapy development.

While this simplified mathematical exercise does not reflect the complexities of a full-scale clinical trial, it does suggest that sponsors should consider coverage of both baseline and comparator therapies for all trial participants in particular instances — not only to potentially reduce costs, but also to improve access to care and shorten therapy development timelines. Ultimately, this may help drive greater participation in clinical trials by patients who would not participate otherwise.

Overall, participation in clinical trials remains limited. While several solutions are being explored (e.g., improving access/education, alleviating indirect expenses), one area that is gaining additional attention is the financial strain that participation in trials may place on patients. Patients are concerned about lack of or lapses in insurance coverage. By opting to cover baseline therapy for trial participants, sponsors may be able to drive approximately $16 million to $144 million in cost savings per 100 patients through mitigation of trial delays and eliminating the need for backfilling while also improving their reputation as a sponsor of choice. Beyond benefits to sponsors, there are a host of benefits to patients who can stay in trials without fear of financial burden and help drive medicine forward for those who come after them.

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Endnotes

[1]Journal of Oncology Practice, "Enrollment of Patients With Lung and Colorectal Cancers Onto Clinical Trials." https://ascopubs.org/doi/full/10.1200/JOP.2012.000598

[2]European Medicines Agency, "ICH E6 (R3) Guideline on good clinical practice (GCP)." https://www.ema.europa.eu/en/documents/scientific-guideline/draft-ich-e6-r3-guideline-good-clinical-practice-gcp-step-2b_en.pdf

[3]Clinical Cancer Research, "The Impact of Insurance on Access to Cancer Clinical Trials at a Comprehensive Cancer Center." https://aacrjournals.org/clincancerres/article/16/24/5997/75943/The-Impact-of-Insurance-on-Access-to-Cancer

[4]Journal of Clinical Oncology, "Financial Concerns About Participation in Clinical Trials Among Patients With Cancer." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4872013/

[5]American Society of Clinical Oncology Educational Book, "Financial Toxicity and Equitable Access to Clinical Trials." https://ascopubs.org/doi/10.1200/EDBK_100019

[6]Journal of Medical Internet Research, "Online Patient Recruitment in Clinical Trials: Systematic Review and Meta-Analysis." https://pubmed.ncbi.nlm.nih.gov/33146627/

[7]Clinical Trials, "Key cost drivers of pharmaceutical clinical trials in the United States." https://pubmed.ncbi.nlm.nih.gov/26908540/

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