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Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

IMPACT REPORT

ANALYSIS & INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

Cost variation and mis-estimation characterize clinical trial budgets, particularly in early phases

Oncology budgets typically over-estimated, while others under-estimated

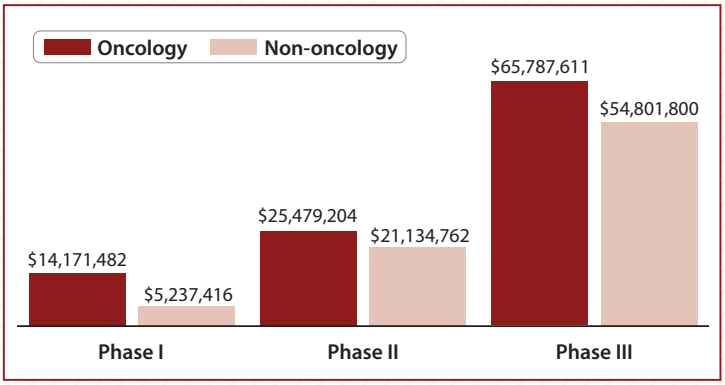
- Average clinical trial budgets exceed $65 million for Phase III oncology protocols and $54 million for non-oncology protocols.
- From Phase I to Phase III, the average number of full-time equivalent employees involved more than triples for oncology and quintuples for non-oncology protocols.
- Phase II and III oncology clinical trial budgets per enrolled patient are nearly double those for non-oncology trials.
- Sponsors typically over-estimate clinical trial budgets for oncology protocols and under-estimate those for non-oncology protocols.
- The widest difference between planned and actual clinical trial budgets is in Phase I.
- There is a high positive correlation between the number of countries in which a sponsor executes a protocol and the clinical trial budget.

Facing limited resources and increasing operating and workforce-related costs across expanding drug development portfolios, sponsor companies are seeking ways to reign in clinical trial costs. At the same time, protocol designs continue to become more complex, resulting in higher levels of inefficiency, greater patient recruitment and retention challenges, and unplanned and unbudgeted disruptions.

Based on the results of a recent working group study, this *Tufts CSDD Impact Report* examines clinical trial budgets and offers insight into the factors driving commonly observed variation and cost.

Clinical trial budgets now exceed $65 million for Phase III oncology protocols and $54 million for non-oncology protocols

Mean actual clinical trial budget per protocol



Source: Tufts Center for the Study of Drug Development

- The average Phase III clinical trial budget for an oncology protocol is more than twice that of Phase II and nearly five times that of Phase I.
- For a non-oncology protocol, the average Phase III clinical trial budget is more than 10 times larger than that for Phase I.
- As non-oncology protocol scope increases in later stage studies, the average clinical trial budget approaches that of oncology.

From Phase I to III, mean number of FTEs triples for oncology and quintuples for non-oncology protocols

Protocol design characteristics by phase

	Phase I*		Phase II*		Phase III*	
	Oncology	Non-oncology	Oncology	Non-oncology	Oncology	Non-oncology
Total FTEs† managing protocol	31.6	12.8	63.7	49.9	98.1	72.1
Number of countries	2.3	1.7	7.4	5.8	21.2	11.3
Number of sites per country	6.0	2.8	3.8	6.4	5.1	7.0
Total patients completing protocol	62.8	42.9	76.1	199.6	382.6	414.9
Total data points collected per protocol	2,290,299.5	235,141.6	3,073,387.0	1,962,146.2	3,599,157.6	3,549,070.3

* All values represent means, † Full-time equivalents

Source: Tufts Center for the Study of Drug Development

- To manage and execute protocol designs, the average number of FTEs per protocol rises from 31.6 in Phase I to 98.1 in Phase III oncology studies and from 12.8 to 72.1 in non-oncology studies.
- The average number of countries for both oncology and non-oncology protocols rises sharply in Phases II and III, which may reflect patient recruitment challenges.
- Relative scope and data volume demonstrates the ambitious objectives of Phase I oncology protocols.

Phase II and III oncology clinical trial budgets per enrolled patient are as much as double those in non-oncology

Protocol execution characteristics by phase

	Phase I*		Phase II*		Phase III*	
	Oncology	Non-oncology	Oncology	Non-oncology	Oncology	Non-oncology
Patients screened per site	11.6	53.9	13.1	11.7	9.2	23.2
Patients randomized per site	8.7	32.6	6.6	7.9	5.8	15.1
Total visits per patient	18.2	12.2	24.8	15.2	30.0	17.8
Total procedures performed per visit	13.1	12.5	16.4	17.4	13.0	13.4
Clinical trial budget per enrolled patient	$180,862	$138,699	$246,007	$119,035	$183,833	$106,603

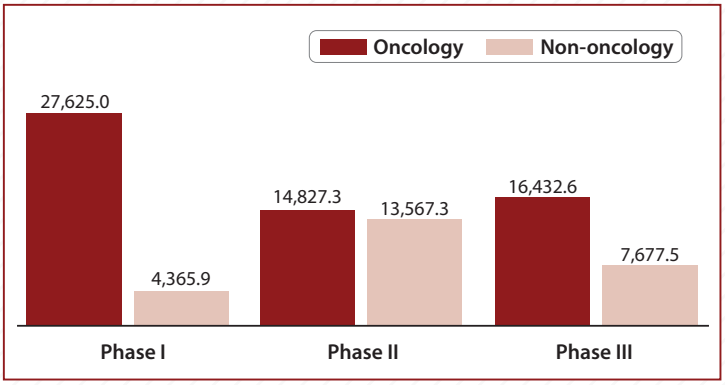
* All values represent means

Source: Tufts Center for the Study of Drug Development

- Site execution burden is higher in oncology trials, as they involve more patient visits, collect more data, and—as past CSDD research indicates—encounter more difficulty recruiting and retaining study volunteers.
- Oncology and non-oncology studies have comparable average numbers of procedures performed per visit, with Phase II protocols being the most demanding.
- In non-oncology studies, the average clinical trial budget per patient is higher in Phase I than in subsequent phases, likely due to the number of safety assessments performed and volunteer compensation.

Phase I oncology trials collect six times more data per patient than non-oncology trials

Clinical data volume per patient



Source: Tufts Center for the Study of Drug Development

- Phase I oncology clinical trials collect an average of 27,265 data points per enrolled patient, compared with 4,365 data points per enrolled patient in a non-oncology trial.
- In Phase II protocols, the average data volume per enrolled patient in oncology and non-oncology studies is comparable.
- In Phase III, the average number of datapoints collected per enrolled patient in oncology studies is more than double that for non-oncology studies.

Sponsors over-estimate clinical trial budgets in oncology and under-estimate those in non-oncology

Clinical trial budget consistency and accuracy

	Oncology		Non-oncology	
	CoV* around mean actual budget	Average difference between actual and planned budget	CoV around mean actual budget	Average difference between actual and planned budget
Phase I	1.35	27.5% below	1.53	9.2% above
Phase II	1.17	10.2% below	1.03	3.8% above
Phase III	.68	12.7% below	.66	2.5% above

* Coefficient of Variation

Source: Tufts Center for the Study of Drug Development

- Variation around mean actual budgets is highest in Phase I and lower in subsequent phases, as sponsors may become more familiar and consistent in managing protocol financials and execution.
- Similarly, the average difference between each protocol's planned versus actual budget is highest in Phase I and lower in subsequent phases.
- Sponsors tend to over-estimate clinical trial budgets in oncology and under-estimate those in non-oncology, with the widest disparities found in Phase I.

Number of countries in which clinical trials are conducted is highly correlated with clinical trial budgets

Protocol design and scope variables correlated with clinical trial budgets*

	Phase I		Phase II		Phase III	
	Correlation coefficient	P value	Correlation coefficient	P value	Correlation coefficient	P value
Number of endpoints	.178	p =.284	.424	**p < .05**	.133	p = .396
Number or eligibility criteria	.082	p = .608	.180	p = .182	.271	**p < .05**
Number of procedures	.241	p = .125	.453	**p < .001**	.201	p =.150
Number of countries	.605	**p < .001**	.682	**p < .001**	.466	**p < .001**
Number of sites per country	.085	p = .605	.022	p = .874	-.154	p = .300
Patients screened per site	-.090	p = .596	.289	**p < .05**	-.058	p = .703
Patients enrolled per site	-.004	p = .982	-.082	p = .552	-.060	p = .692
Data points collected per patient	-.034	p = .852	.136	p = .357	.208	p = .216

* P values **in bold** indicate statistical significance

Source: Tufts Center for the Study of Drug Development

- With few exceptions, there was virtually no significant correlation between protocol design variables and clinical trial budgets, in part due to the high observed level of protocol customization within and between phases.
- Across all phases, there was a high positive correlation between the number of countries in which a sponsor executes a protocol and the clinical trial budget.
- In Phase II, the number of endpoints and number of patients screened per site were positively correlated with clinical trial budgets.

About this study

The data and metrics presented in this report are based on an analysis of 223 protocols provided as part of a working group study comprised of 20 major pharmaceutical, biotechnology, and contract research services companies. The protocols were conducted after 2015 and had to have a primary completion or final database lock date before December 31, 2019. The analysis dataset targeted multiple therapeutic areas, with one-third representing oncology diseases, and was distributed as follows: 25% Phase I protocols, 41% Phase II, and 34% Phase III.

This analysis was conducted by Zak Smith, MA, project manager and data scientist, and Ken Getz, MBA, principal investigator, professor, and executive director, both of Tufts CSDD.

Definition of terms

Clinical trial — A specific type of clinical study in which a medical intervention is tested against a placebo or an active control in human subjects. Clinical study is a broader term that includes other forms of human participatory research, such as pharmacokinetic, epidemiologic, and behavioral studies.

Clinical trial budget — The total direct cost associated with the execution of a clinical trial including study grants; contract research organization (CRO) and vendor payments; clinical supply preparation and distribution costs; patient recruitment and retention expenses; compensation for study volunteers; and the implementation of amendments.

Database lock — Point at which data collected in a clinical trial is deemed final, ready for analysis.

FTEs — Full-time equivalents, a metric used to show what total labor hours equate to in full-time employees.

Phase I — As the name indicates this is the first phase or earliest stage of studies designed to investigate the safety and tolerability of an investigational drug in humans.

Phase II — Studies designed to obtain data on the efficacy of a drug for a particular indication or indications in patients with the disease or condition.

Phase III — Studies conducted among an even larger number of patients with a given disease or condition to gather additional data about efficacy and safety, and to evaluate the value, benefits, and risk of an investigational drug.

Protocol — A plan detailing the methodology of a clinical study.

About the Tufts Center for the Study of Drug Development

The Tufts Center for the Study of Drug Development at Tufts University School of Medicine is a multidisciplinary research center dedicated to optimizing drug development performance, efficiency, and economics through robust, data-driven assessments, analysis, and insight.

Tufts Center for the Study of Drug Development
Tufts University
145 Harrison Avenue | Boston, MA 02111 USA
Phone: (617) 636-2170 | Fax: (617) 636-2425
E-mail: csdd@tufts.edu | Website: csdd.tufts.edu

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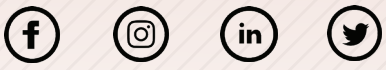

Tufts CSDD Impact Reports are published by the Tufts Center for the Study of Drug Development six times a year; Kenneth I Kaitin, PhD, editor.