VOLUME 24, NUMBER 5 | September/October 2022

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

IMPACT REPORT
ANALYSIS & INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

DCTs substantially increase financial value based on key performance indicators

Decentralized Clinical Trial (DCT) methods increase value by $20 million per drug, if applied in both Phase II and III trials

- Data available on the impact of DCT solutions show a reduction in three factors that can impact drug development financial value—clinical phase cycle times, screen failure rates, and the number of substantial protocol amendments.
- Applying DCT methods in Phase II clinical trials results in an increase in value of $8.6 million, on average, per investigational drug, or nearly a five-fold return on investment (ROI).
- In a portfolio of Phase III drugs, DCT methods increase value by $41 million per drug, with a 13-fold ROI.
- There is an increase in value of $20.4 million per Phase II investigational drug when drug developers apply DCT methods to both Phase II and Phase III trials.
- Reductions in cycle time, measured from the start of one phase to the start of the next, have the greatest impact on value in both Phase II and Phase III trials.

More than a decade ago, sponsors began deploying virtual and remote solutions to support clinical trial execution. The COVID-19 pandemic, however, catalyzed rapid and extensive adoption of these solutions to reduce the risk of transmitting infection, minimize delays and disruptions, accelerate the collection of clinical research data, facilitate participant access to clinical studies, and lower participation burden.

Commonly referred to as decentralized clinical trials (DCTs), sponsors and contract research organizations (CROs) are now looking for insights into optimizing the value of DCT deployments. This *Tufts CSDD Impact Report* presents the results of an initial Tufts CSDD study quantifying the net financial return on DCT investment. Value was measured by changes in expected net present value (eNPV). The study looked at three factors for which data were available that can impact eNPV.

Application of DCT methods results in performance improvement in three factors studied

Factors impacted by DCTs

	Phase II		Phase III	
Performance indicators	DCT	Non-DCT	DCT	Non-DCT
Substantial protocol amendments	2.4	3.3	3.2	3.4
Screen failure rate	24.1%	31.5%	20.1%	29.9%
Phase duration (months)	27	30	28	31

Source: Tufts Center for the Study of Drug Development

- Tufts CSDD and Medable, Inc. data indicate that the application of DCT methods results in a reduction of 27% in substantial protocol amendment filings for Phase II trials and a reduction of 6% for Phase III trials.
- Screen failure rates are reduced, on average, by 7.4% for Phase II trials and by 9.8% for Phase III trials with DCT methods.
- Tufts CSDD benchmark data indicate an approximate 10% reduction in Phase II and Phase III trial phases with the application of DCT methods.

Applying DCT methods across all Phase II trials yields a nearly five-fold ROI per investigational drug

Increases in eNPV and ROI for Phase II DCTs by the reduction in cycle time

Cycle time reduction (months)	eNPV delta	eNPV delta as percent of base eNPV	ROI
1	$3,042	1.0%	1.61x
2	$5,884	1.9%	3.11x
3 (base analysis)	$8,750	2.8%	4.62x
4	$11,641	3.7%	6.15x
5	$14,588	4.7%	7.69x
6	$17,499	5.6%	9.25x

Notes: Costs and returns discounted to the start of Phase II testing (Thousands of year 2020 US $); ROI = eNPV delta/implementation cost

Source: Tufts Center for the Study of Drug Development

- For the base case analysis, the application of DCT methods results in an increase in sponsor eNPV of $8.8 million per investigational drug, or 2.8% of the base case non-DCT total eNPV.
- The ROI in the base case is nearly five times the investment in DCT deployments.
- The increase in eNPV is approximately twice as high as the base case if cycle time is reduced by six months.

For Phase II trials, cycle time reductions had the greatest impact on value

Phase II DCT value impacts for individual factors

Performance indicators	eNPV delta	eNPV delta as percent of base eNPV	ROI
Amendments only	-$1,014	-0.3%	-0.54x
Screen failure only	-$148	<-0.1%	-0.08x
Cycle time only	$7,121	2.3%	3.76x
Screen failure plus amendments	$224	<0.1%	0.12x
Amendments plus cycle time	$7,497	2.4%	3.96x
Screen failure plus cycle time	$8,374	2.7%	4.43x

Notes: Costs and returns discounted to the start of Phase II testing (Thousands of year 2020 US $); ROI = eNPV delta/implementation cost

Source: Tufts Center for the Study of Drug Development

- Considered individually, the mean reduction in number of protocol amendments and in screen failure rates for Phase II trials result in negative ROI of 54% and 8%, respectively, after accounting for implementation costs.
- A three-month reduction in cycle time alone, however, increases value per investigational drug by $7.1 million for Phase II and represents a nearly four-fold increase in ROI.
- DCT methods increase value if any two of the factor effects are included. The ROI is 12% if only protocol amendments and screen failure rates are accounted for, but the ROI is approximately four-fold if cycle time is included with either factor.

Applying DCT methods across Phase III trials yields, on average, a 13-fold ROI per drug

Increases in eNPV and ROI by the reduction in Phase III cycle time

Cycle time reduction (months)	eNPV delta	eNPV delta as percent of base eNPV	ROI
1	$17,258	1.3%	5.51x
2	$29,157	2.2%	9.33x
3 (base analysis)	$41,158	3.2%	13.17x
4	$53,263	4.1%	17.04x
5	$65,471	5.0%	20.94x
6	$77,785	6.0%	24.88x

Notes: Costs and returns discounted to the start of Phase III testing (Thousands of year 2020 US $); ROI = eNPV delta/implementation cost

Source: Tufts Center for the Study of Drug Development

- For the base case analysis, the application of DCT methods results in an increase in sponsor eNPV of $41.2 million per investigational drug, or 3.2% of the base case non-DCT total eNPV.
- Accounting for the cost of implementing DCT methods, the ROI in the base case is 13 times the investment cost.
- The increase in value from applying DCT methods to Phase III trials, as measured by eNPV, is 89% higher than for the base case if cycle time is reduced by six months.

For Phase III trials, cycle time reductions had the greatest impact on value

Phase III DCT value impacts for individual factors

Performance indicators	eNPV delta	eNPV delta as percent of base eNPV	ROI
Amendments only	-$2,049	-0.2%	-0.66x
Screen failure only	$5,226	0.4%	1.67x
Cycle time only	$33,323	2.6%	10.66x
Screen failure plus amendments	$5,460	0.4%	1.75x
Amendments plus cycle time	$33,560	2.6%	10.74x
Screen failure plus cycle time	$40,921	3.1%	13.09x

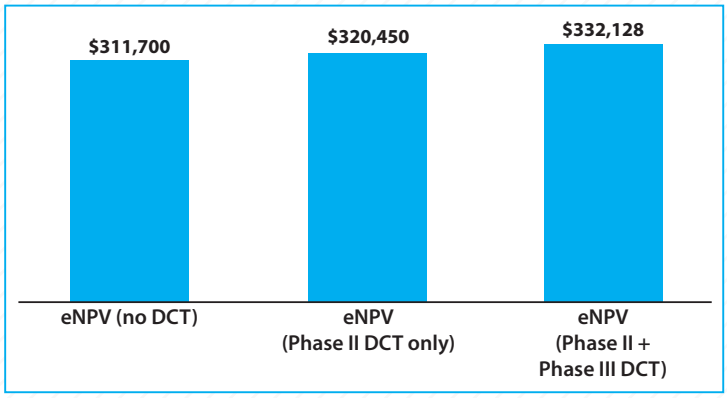
Notes: Costs and returns discounted to the start of Phase III testing (Thousands of year 2020 US $); ROI = eNPV delta/implementation cost

Source: Tufts Center for the Study of Drug Development

- The mean reduction in Phase III protocol amendments alone results in a negative ROI of 66% after accounting for implementation costs, but a reduction in screen failure rates alone is associated with a 67% ROI.
- A three-month reduction in cycle time alone increases value per investigational drug by $33.3 million for Phase III and represents a nearly 11-fold ROI.
- The ROI is 75% if only protocol amendments and screen failure rates are considered, but the ROI is approximately 11-fold if cycle time is included with protocol amendments and approximately 13-fold when cycle time and screen failure rates are considered.

Applying DCT methods across both Phase II and Phase III trials increases total value

Comparison of eNPV with and without DCT methods and when applied to all Phase II and III trials



Notes: All costs and returns discounted to the start of Phase II testing (Thousands of year 2020 US $)

Phase III DCT impact weighted by the likelihood of entering the phase, given that the drug has entered Phase II (35.5%)

Source: Tufts Center for the Study of Drug Development

- The increase in value for Phase II trials with DCT methods versus trials with no DCT methods is $8.8 million, and $20.4 million per drug when DCT methods are used for both Phase II trials and the minority of drugs that will enter Phase III.
- The increase in eNPV when applying DCT methods to both Phase II and Phase III trials is 6.6% of the base eNPV (i.e., where there is no use of DCT methods).
- The ROI from implementing DCT methods for both Phase II and Phase III trials is 6.81.

About this study

Tufts CSDD developed an expected net present value (eNPV) model of the cash flows for new drug development and commercialization to evaluate the net financial benefits of employing DCT methods. The measure of DCT financial value is the increment in eNPV that occurs, on average, when DCT methods are used compared to when they are not. The model is populated with base case parameter values taken from prior Tufts CSDD published studies (e.g., DiMasi et al., *Journal of Health Economics*, 2016), Tufts CSDD benchmark data from pre-COVID clinical trials, and Medable data on DCT projects. A ROI metric was also calculated as the ratio of the increment in eNPV to the cost of implementing DCT methods.

Joseph A. DiMasi, PhD, director of economic analysis and research associate professor at Tufts CSDD, was the principal investigator for this study. Zachary Smith, MA, project manager and data scientist, and Kenneth A. Getz, MBA, executive director and research professor, also contributed to this report, both of Tufts CSDD. The full study, co-authored with Ingrid Oakley-Girvan, Andrew Mackinnon, Mary Costello, and Pamela Tenaerts, all of Medable, Inc., is in press at the peer review journal Therapeutic Innovation & Regulatory Science (TIRS). *This research was supported, in part, by a grant from Medable, Inc.*

Definition of terms

Decentralized Clinical Trial (DCT) — Clinical trials executed virtually or remotely, through the use of telemedicine, mobile devices, smart phones, portable equipment, mobile and local healthcare providers. Generally, these trials are conducted at the participant's home or at conveniently located areas instead of at an investigative site or research facility. They are deployed as hybrid executional approaches to reduce the number of in-person participant visits to investigative sites or as fully virtual approaches with no in-person participant visits.

Expected net present value (eNPV) — A commonly used and widely recognized, risk-adjusted financial modeling technique for evaluating the value of investment project portfolios. This method accounts for research and development investment cash flows, risks in reaching the marketplace, costs of commercialization, and projected sales. A positive eNPV indicates that an investment is, from a purely financial perspective, worth pursuing.

Screen failure rate — Screen failures occur when research staff put potential participants through a screening process to ensure they fit the inclusion criteria for a clinical trial, only for those potential participants to not enroll in the trial. This is problematic because research organizations must commit personnel, budgets, and resources to identifying and screening potential trial participants.

Substantial protocol amendment — Changes made to the protocol, in all countries where it is executed, requiring suspending enrollment, obtaining internal approval followed by approval from an ethical review board or regulatory authority, and re-consenting study volunteers.

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.

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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.