Society for Clinical Research Sites

The Future of Clinical Trials: Trends, Challenges and Opportunities

Site Solutions Summit™

SPEAKER

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FACULTY DISCLOSURE

In compliance with ACCME Guidelines, I hereby declare:

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Ken Getz, Tufts Center for the Study of Drug Development, Tufts University School of Medicine

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MOREHOUSE SCHOOL OF MEDICINE

Criteria for AWARDING CONTACT HOURS

Applicants must be present during the “live” event, contact hours are not issued for recordings
Applicants must attend the activity the whole time, missing no more than ten minutes of the activity
Applicants must complete the post-meeting survey with a score of at least 70%
Applicants must complete the post meeting survey evaluation questions

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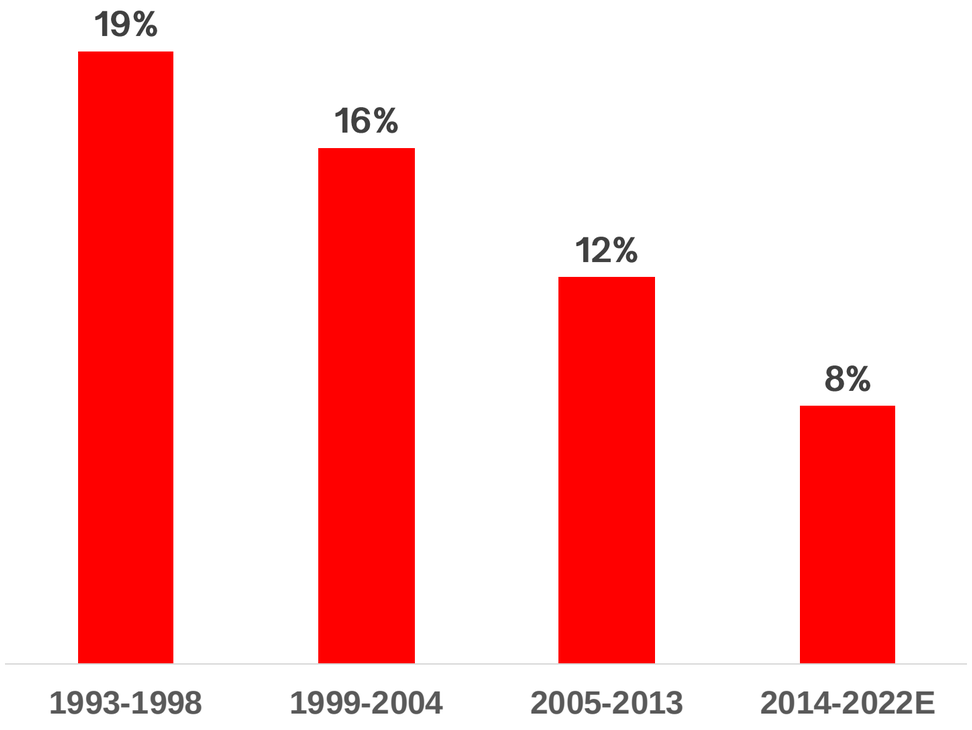
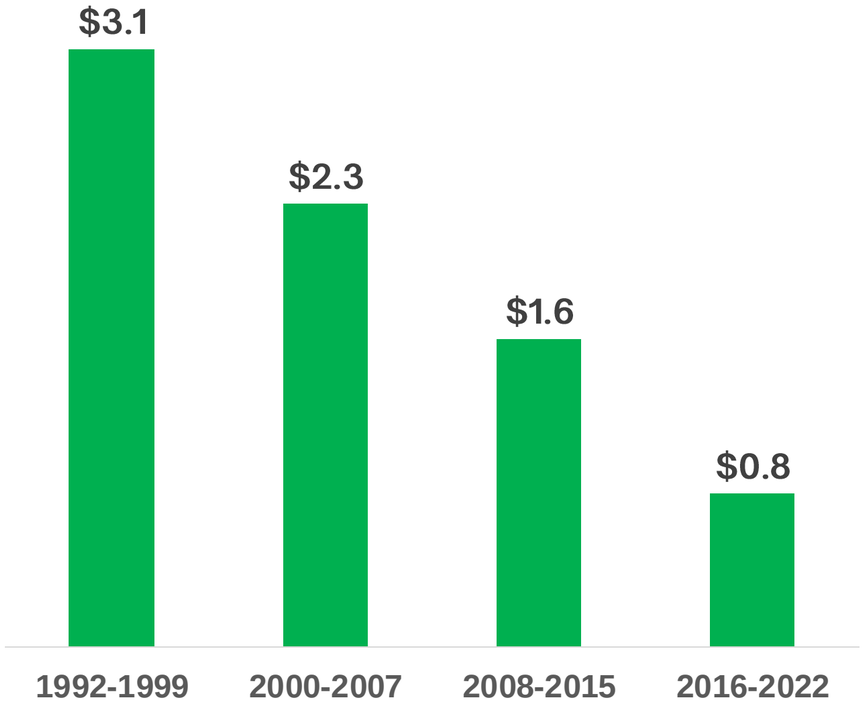
A Mic-Drop Moment!

Drug Development Success Rates
(Percent of IND Filings receiving FDA Approval)



Mean Daily Sales by Launch Year



Source: Tufts CSDD

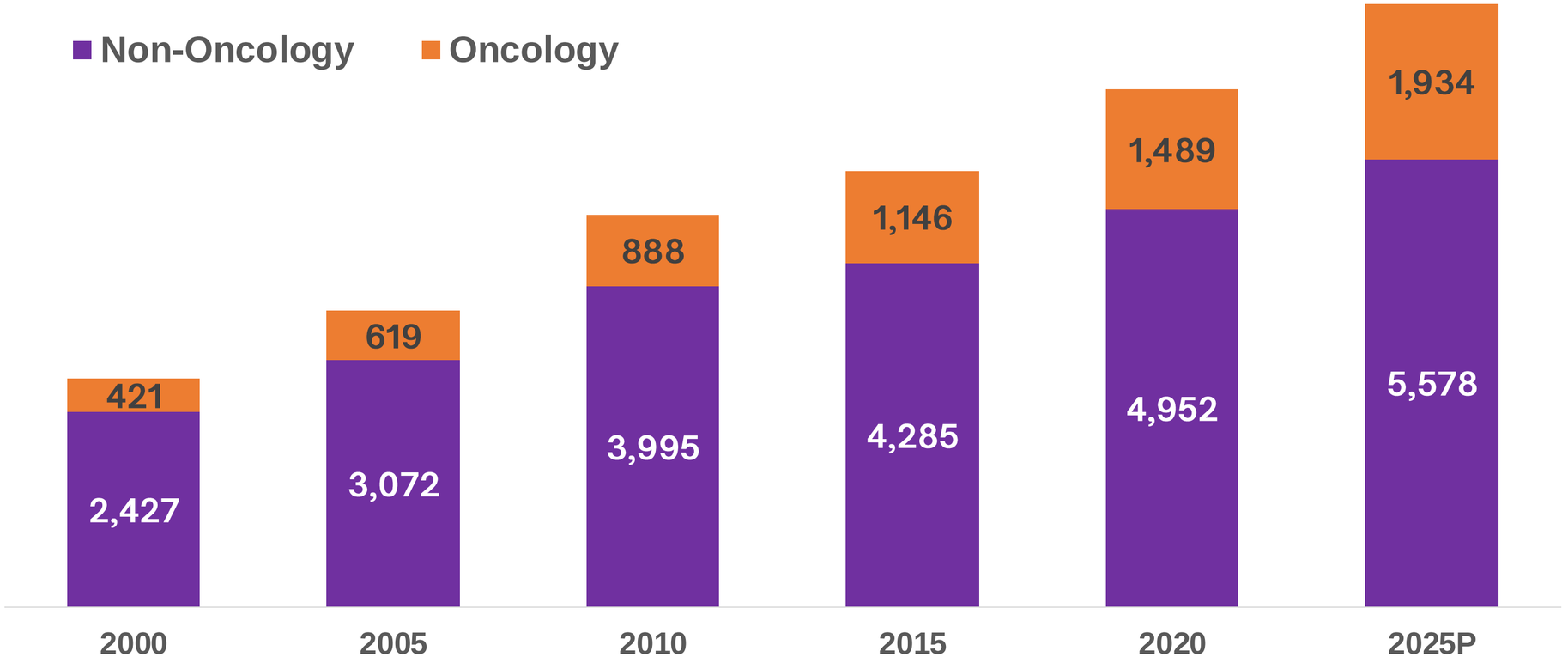
Agenda

Site Solutions Summit™

- Overview of Major Trends
- Acute and Chronic Root Causes
- Optimization Opportunities

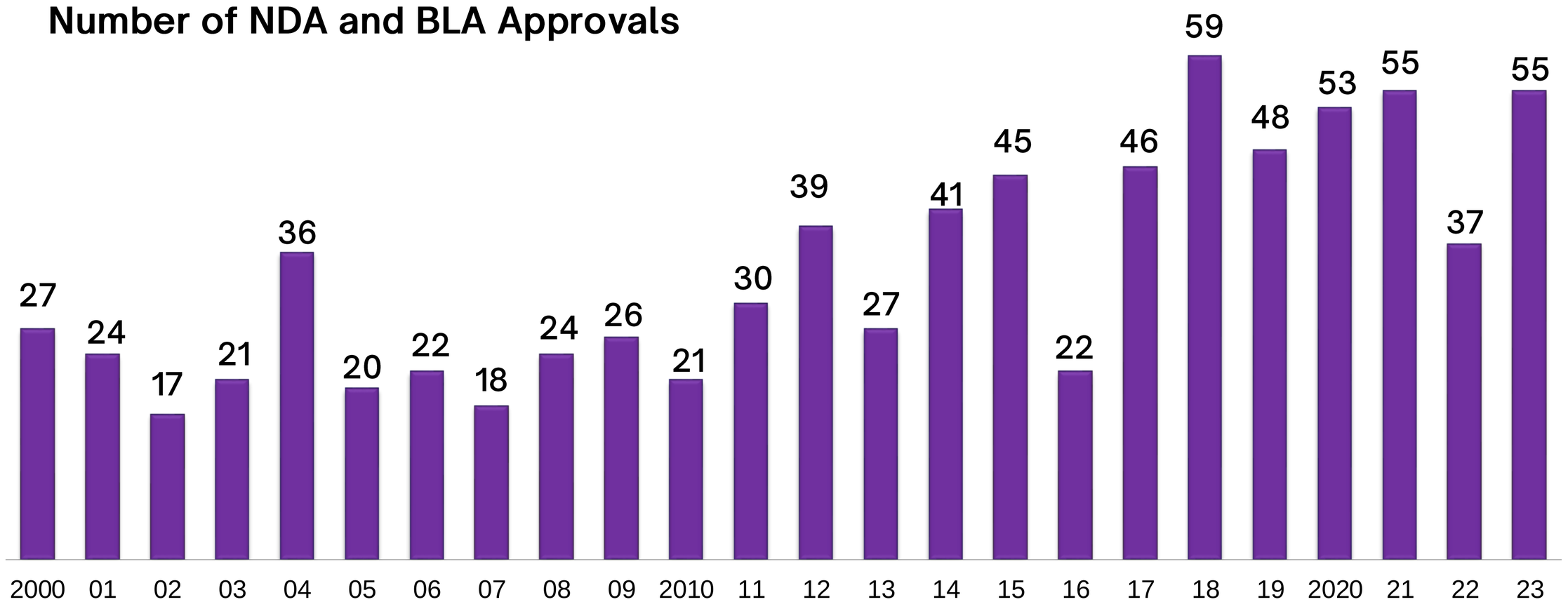
Strong Overall Global Pipeline Growth

Total Drugs and Biologics in Phase I – III Clinical Testing



Source: PharmaProjects; Evaluate Pharma, Tufts CSDD

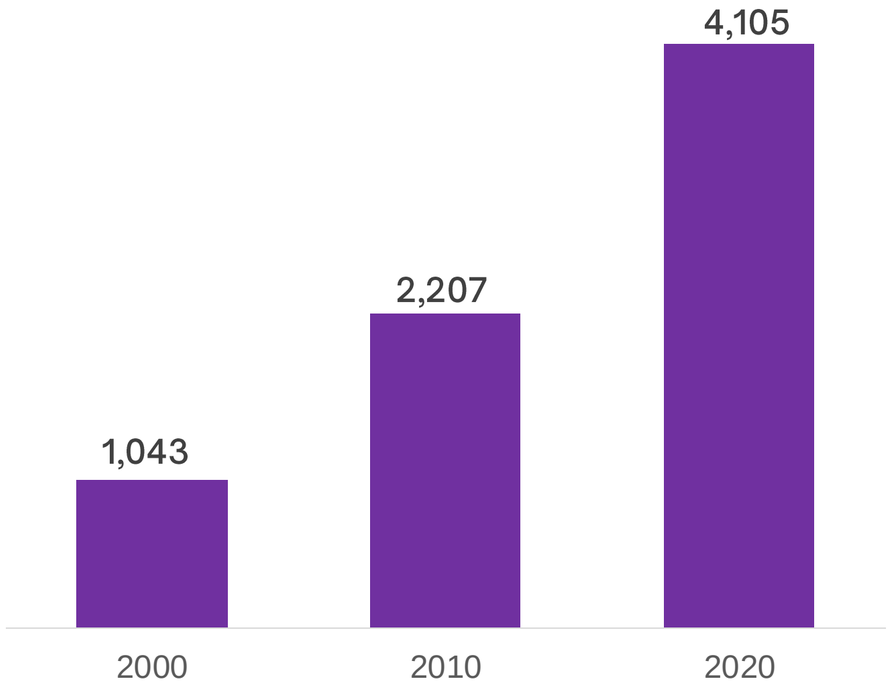
A Highly Productive Enterprise



Source: Tufts CSDD; CDER (FDA)

Changing Global Pipeline Composition

Companies with At Least One Molecule in Clinical Testing



Changing Pipeline Composition

	Percent of Drugs in R&D that are Personalized Therapies	Percent of Drugs in R&D Targeting Rare Diseases
2000	3%	9%
2010	19%	14%
2020	61%	34%

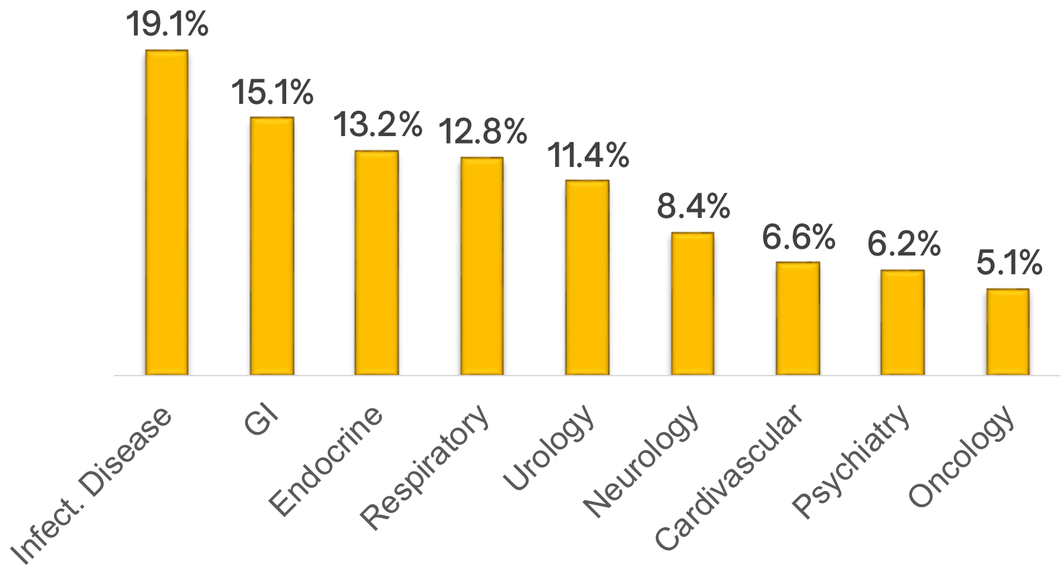
Source: PharmaProjects; Evaluate Pharma, Tufts CSDD

Drug Development Risk: by Phase and TA

Phase Transition Probabilities

	1993 to 1998	1999 to 2004	2005 to 2013
Phase I - II	67%	64%	58%
Phase II - III	41%	39%	34%
Phase III - Submission	63%	66%	62%

Overall Probability of Achieving Regulatory Approval



Source: Tufts CSDD

Clinical Trial Durations by Phase

Time Period	Mean Trial Duration (months) (Protocol Approval to DBL)	Coefficient of Variation
Phase I		
2008-2013	13.8	1.59
2014-2018	14.8	1.51
2018 - 2021	20.3	1.29
Phase II		
2008-2013	27.1	.88
2014-2018	30.2	.85
2018 - 2021	40.6	.98
Phase III		
2008-2013	26.8	.83
2014-2018	28.5	.75
2018 - 2021	39.4	.91

Source: Tufts CSDD; N = 1,329 protocol

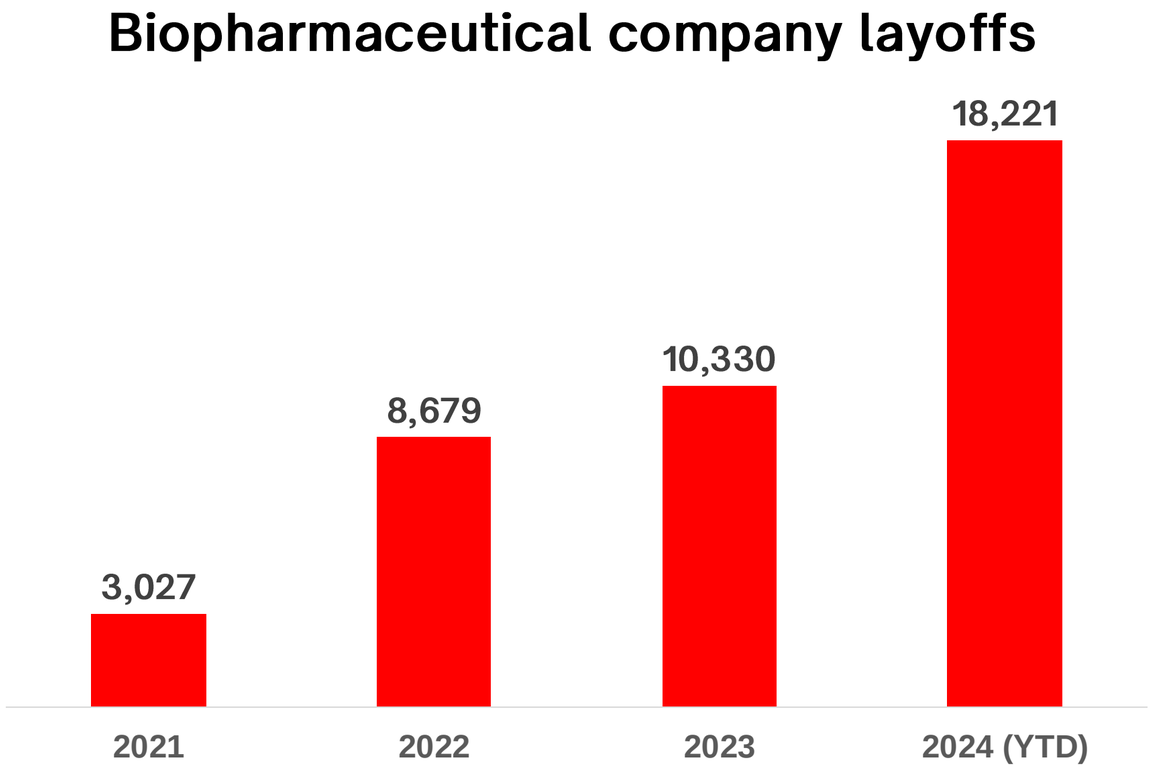
Declining RODI and Unprecedented Pricing Pressures

	Mean Peak Sales per Approval ($US Millions)	Total Global R&D Spend ($US Billions)	Mean Percent of Total Sales Invested in R&D	Return on R&D Investment
2005	$757	$94.2	18.2%	12.4%
2010	$816	$127.4	18.4%	10.1%
2020	$396	$159.4	20.9%	3.1%

In 2023, rare disease treatments for 8.4 million people (6% of all people living with diseases) will cost the US health care system $2.2 trillion dollars, more than one-third (34%) of the total pharmaceutical therapies budget.

Sources: Statista, Evaluate Pharma, Deloitte, Oliver Wyman

Global Economic Conditions



- High inflation and soft consumer demand
- Patent Cliff
- Pricing regulation
- Budget pressures
- Supply chain shortages
- Volatile climate change and global unrest

Sources: BIO

Trends in Annual Clinical Trials Initiated

Declining Number of Trial Starts

	Phase I	Phase II	Phase III
2017	1,601	1,779	916
2019	2,059	1,921	1,020
2021	2,169	2,185	1,102
2023	1,893	1,848	946
2025F	1,656	1,533	841

Changing Mix by TA

TOP TAs	2022	2024
Oncology	42.2%	38.6%
CNS	16.6%	17.8%
Infectious Diseases	8.4%	5.5%
Immunology	6.7%	4.5%
CV	5.7%	5.0%
Endocrine	3.3%	6.1%

Source: IQVIA, Tufts CSDD

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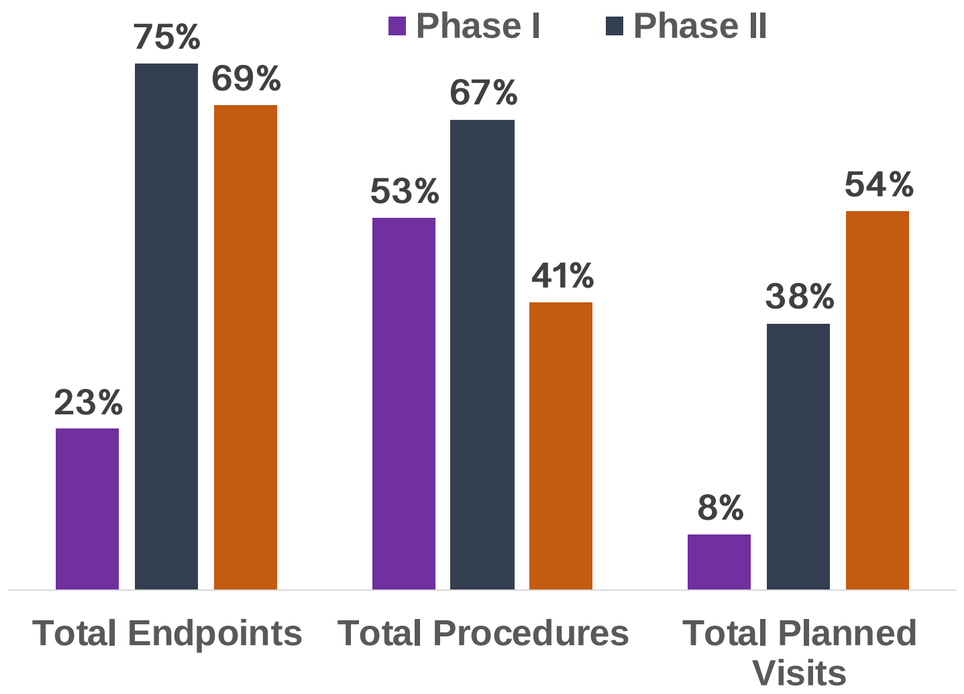
Scientific and Operating Customization

Protocol Design Practices

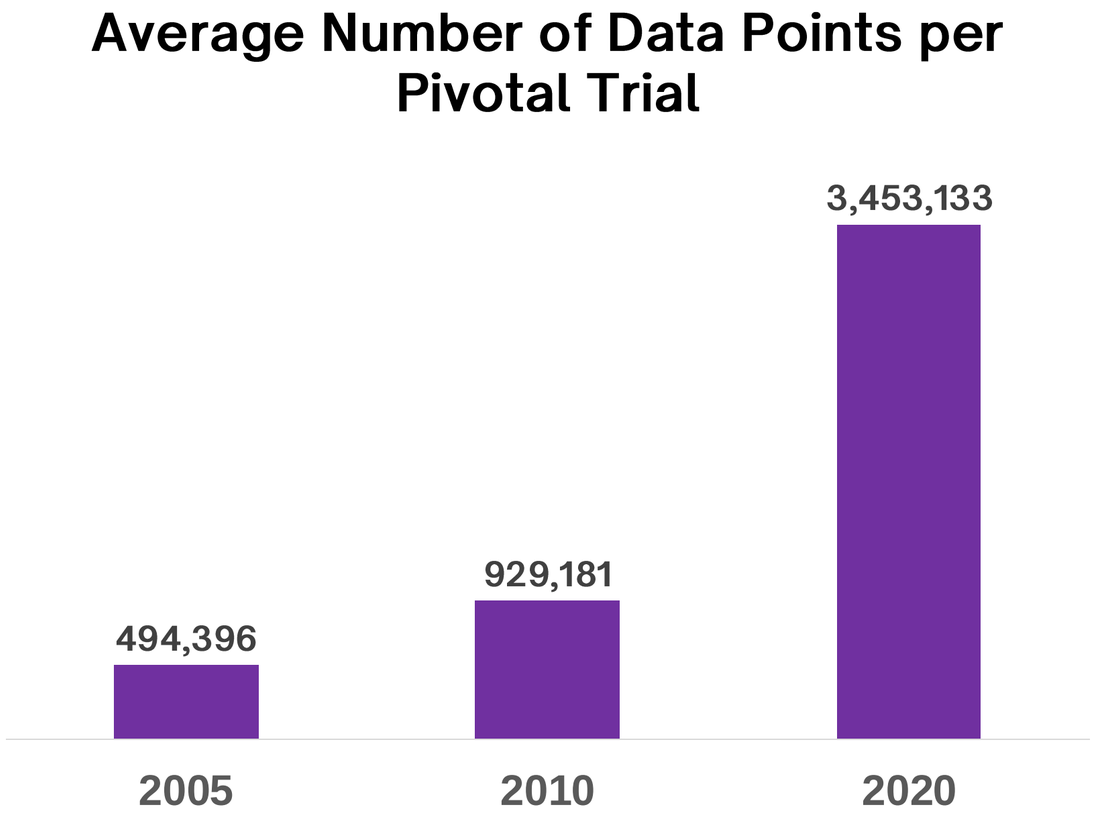
Phase III Pivotal Trials *(Means)*	Overall	
	2010	2020
Total Endpoints	13	22
Total Eligibility Criteria	34	30
Total Procedures	187	263
Total Countries	9	15
Total Investigative Sites	65	104
Procedures per Visit	11	13
Total Patients Randomized	597	632

Growth in Customization
(2010-2020)



Source: Tufts CSDD

Clinical Data Volume and Data Diversity



	Mean Number of Primary Data Sources per Pivotal Trial Protocol	Percent of Drugs in the Pipeline Relying on Biomarker and Genetic Data
2005	1.3	5%
2010	1.9	23%
2020	4.2	64%

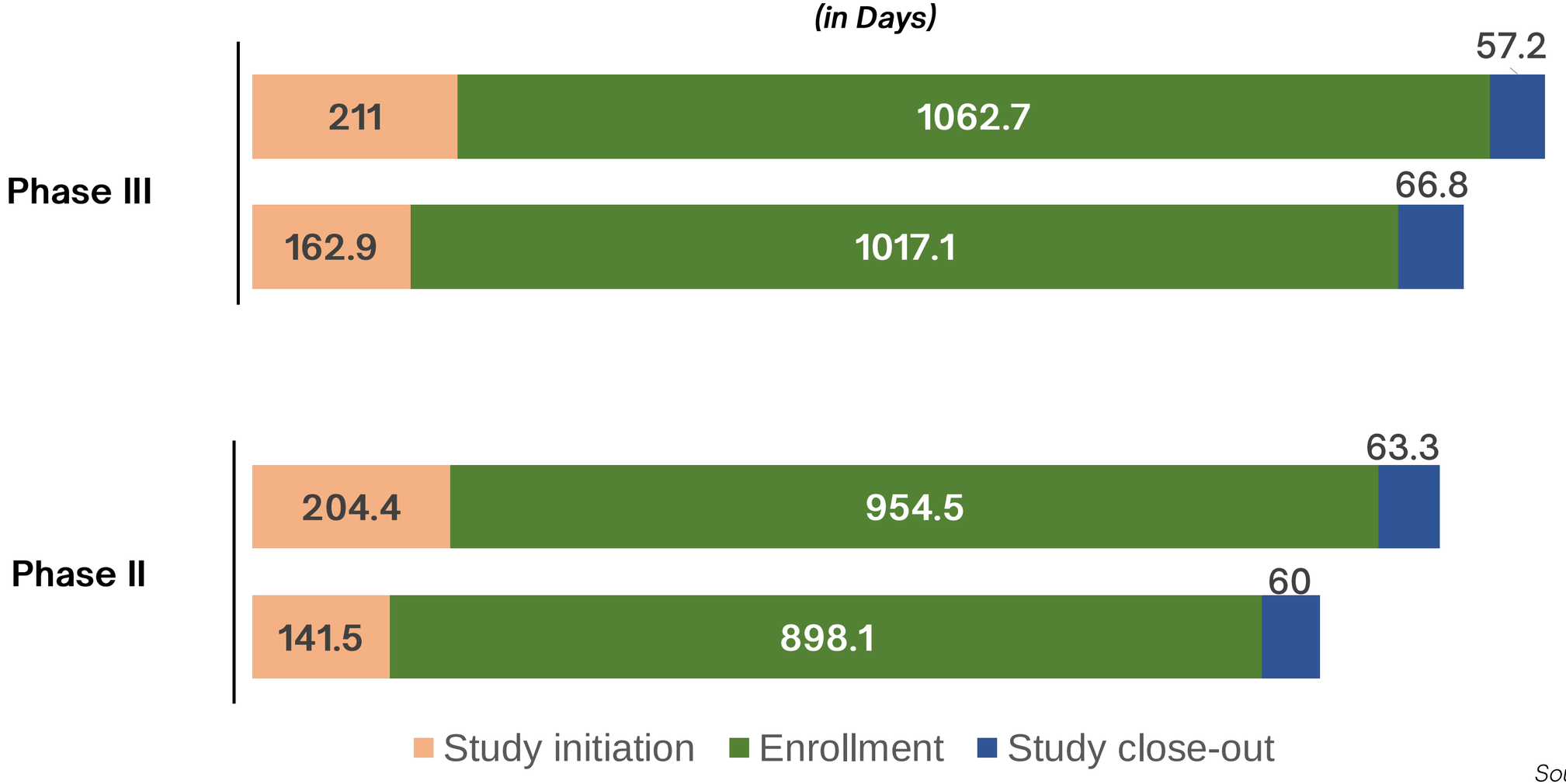
Source: Tufts CSDD

Variation in Design Practices by Patient Community

Phase II/III Protocols *(Mean Number)*	Non-Oncology	Oncology	Rare Diseases
Total Endpoints	21.4	15.3	12.9
Total Eligibility Criteria	31.0	29.8	28.9
Total Procedures	242.0	315.0	301.6
Total Countries	8.4	13.1	9.7
Total Investigative Sites	54.2	67.6	24.2
Procedures per Visit	14.4	11.9	12.1
Total Patients Randomized	373.1	431.1	223.7
Total Data Points Collected	2,732,132	2,563,973	1,599,282

Source: Tufts CSDD, 2022

A More Granular Look at Clinical Trial Durations



Source: Tufts CSDD

Variation in Trial Performance by Patient Community

Phase II/III Protocols *(Mean Days and Percents)*	Non-Oncology	Oncology	Rare Diseases
Total Duration (Final Protocol to DBL)	1,080.9	1,598.7	1,304.8
Study Initiation (Final Protocol to FPFV)	146.4	148.3	173.3
Enrollment Duration (FPFV – LPLV)	852.1	1,327.2	1,073.6
Close-Out Duration (LPLV – DBL)	59.9	68.5	61.4
Randomization Rate (Enrolled/Screened)	70.9%	67.1%	76.3%
Completion Rate (Completed/Enrolled)	80.0%	31.4%	48.8%

Source: Tufts CSDD, 2022

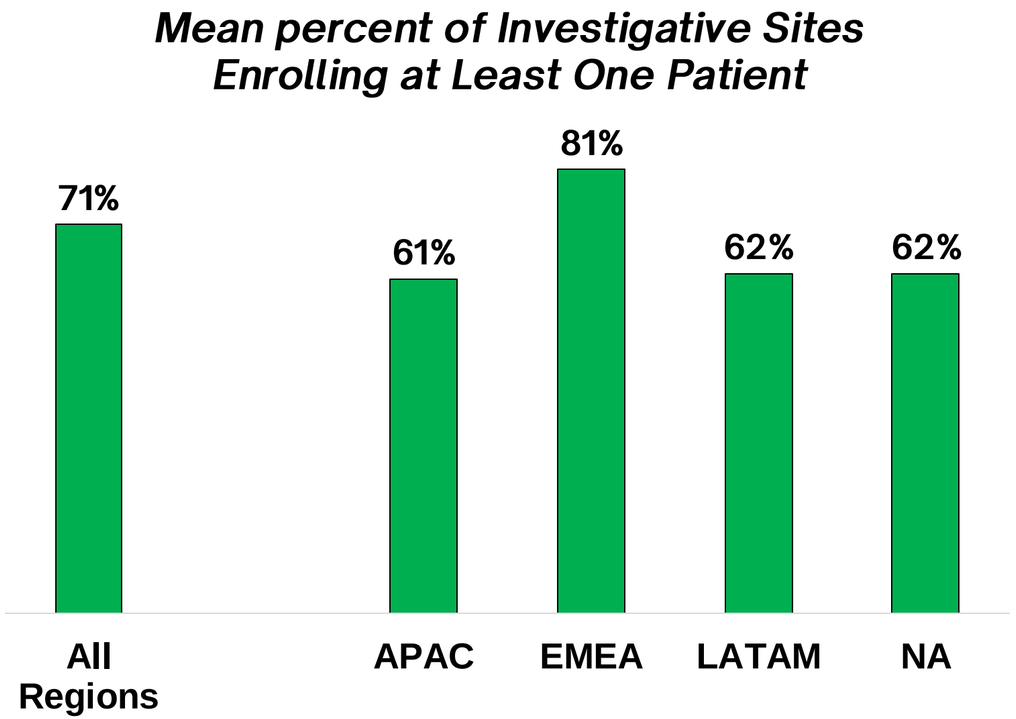
Trends in Substantial Protocol Amendments

	2013-2015 *(N=836)*		2018-2021 *(N=952)*	
	Proportion with at least 1 substantial amendment	Mean number of substantial amendments	Proportion with at least 1 substantial amendment	Mean number of substantial amendments
Phase I	52%	1.8	67%	3.1
Phase II	77%	2.2	89%	3.3
Phase III	66%	2.3	82%	3.5

- Estimated average direct cost to implement a single amendment is nearly $1million and add 3 months of unplanned time
- Average time to implement ands amendment has tripled since 2010
- Time from identifying the need to and to obtaining last oversight approval is 260 days on average
- The mean time during which sites are operating with different version of the protocol is 215 days

Investigative Site Burden

Site Enrollment Achievement Rates



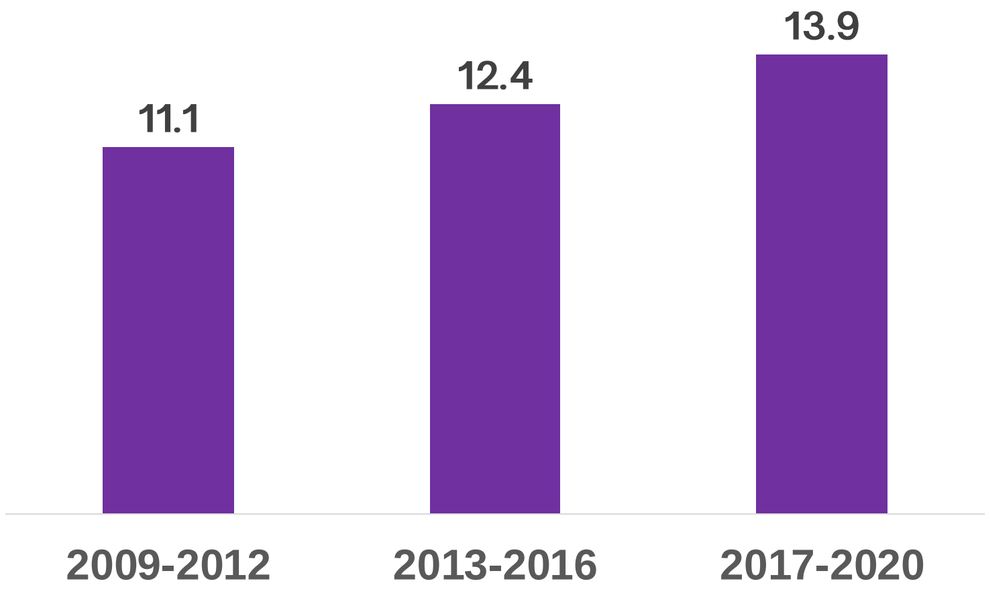
Enrollment Experience by Select Therapeutic Areas

Phase II/III Trials	Randomization Rates		Completion Rates	
	2019	2023	2019	2023
Cardiovascular/ Metabolic	84%	66%	93%	61%
CNS/Neurosciences	25%	16%	74%	66%
Inflammatory Diseases	75%	68%	81%	54%
Oncology	63%	56%	69%	22%

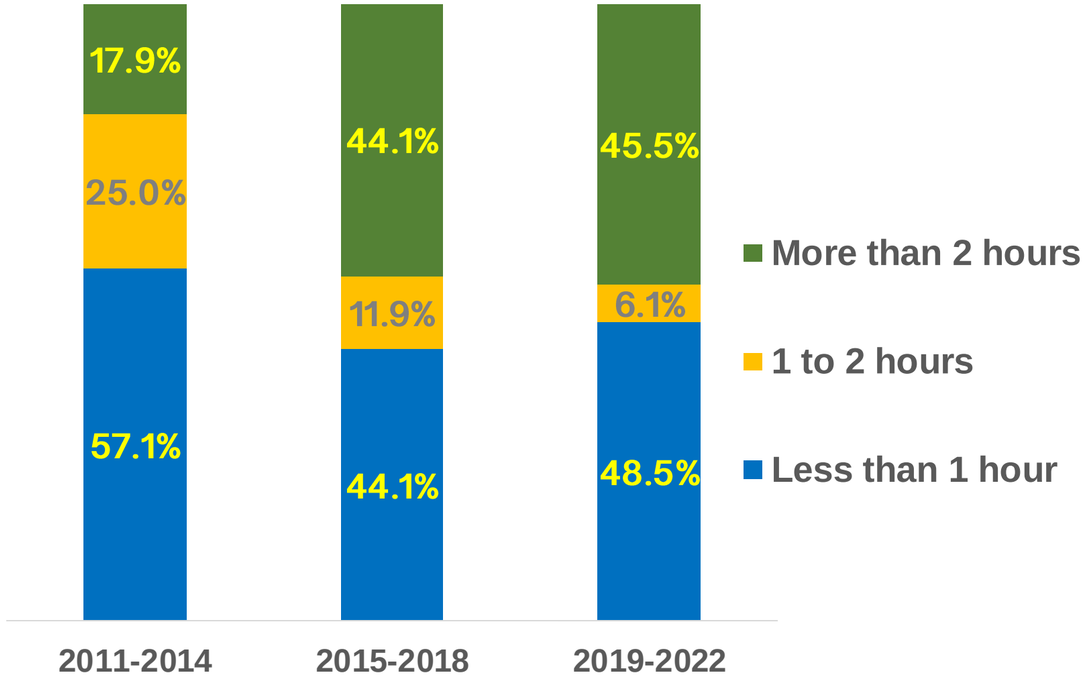
Source: Tufts CSDD; n= 11,000 global investigative sites

Patient Participation Burden

Mean Procedures per Patient Visit
(Phase II & III protocols, All TAs)



Distribution of Protocols by Average Visit Duration



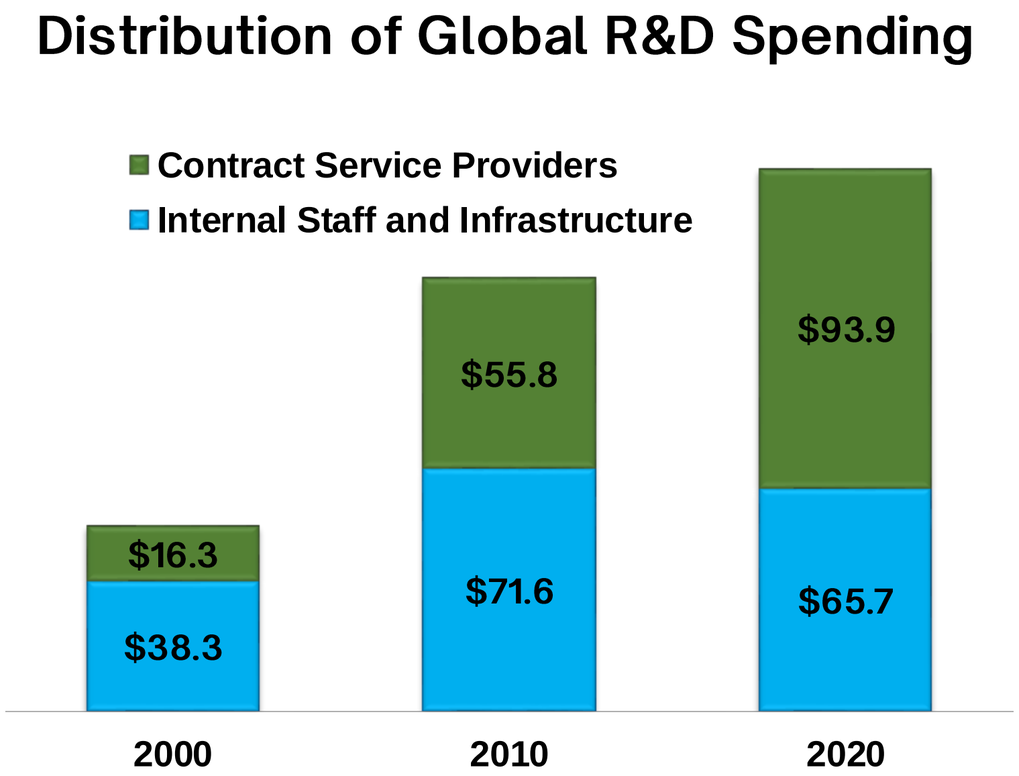
Source: Tufts CSDD

Demographic Disparities in Pivotal Trials

1,165 pivotal trials for all drugs and biologics approved between 2007 and 2021	Distribution	Proportional disparity in pivotal trials, based on disease prevalence	Percent of total pivotal trials in which a proportional disparity >20% is observed
Black/African Descent	8.6%	-64.2%	78%
Asian	9.6%	-31.7%	55%
Other	4.1%	-73.3%	80%
White	77.2%	+12.9%	10%
Hispanic/Latino	13.1%	-32.1%	57%

Source: Tufts CSDD

Customization via ‘Fragmentation’ (Intermediaries)



- On average, Investigative sites respond to 81 feasibility assessment and 30 qualification visit requests per year

- The global community of investigative sites spent an estimated $350 million annually responding to and completing feasibility and qualification visit assessments in 2023

Source: EvaluatePharma; Tufts CSDD

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Three Primary Optimization Areas

Patients
(Individuals and Communities)

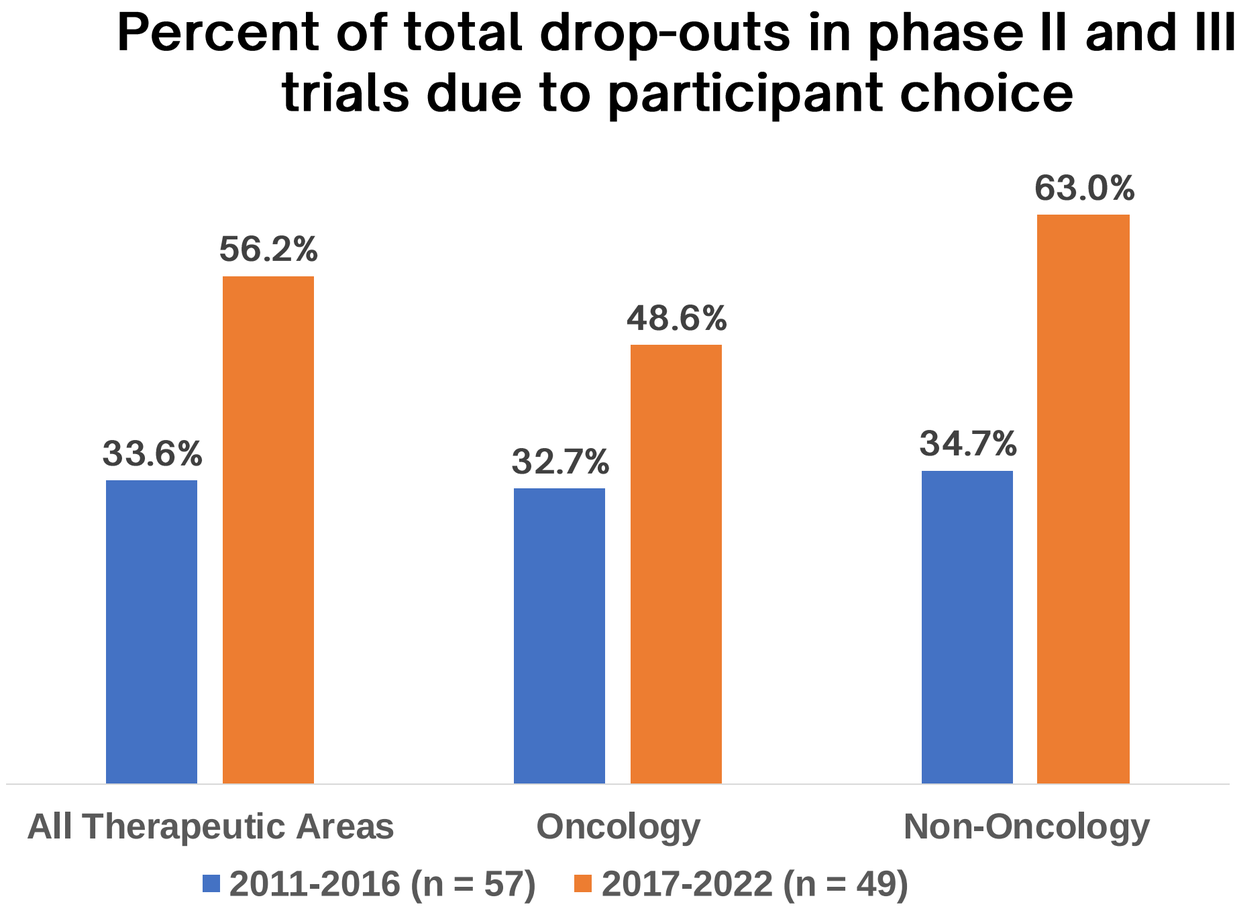
Data
(Quality and Analytics)

Risk
(Orientation and Sharing)

Integrated, Agile, Coordinated, Continuous

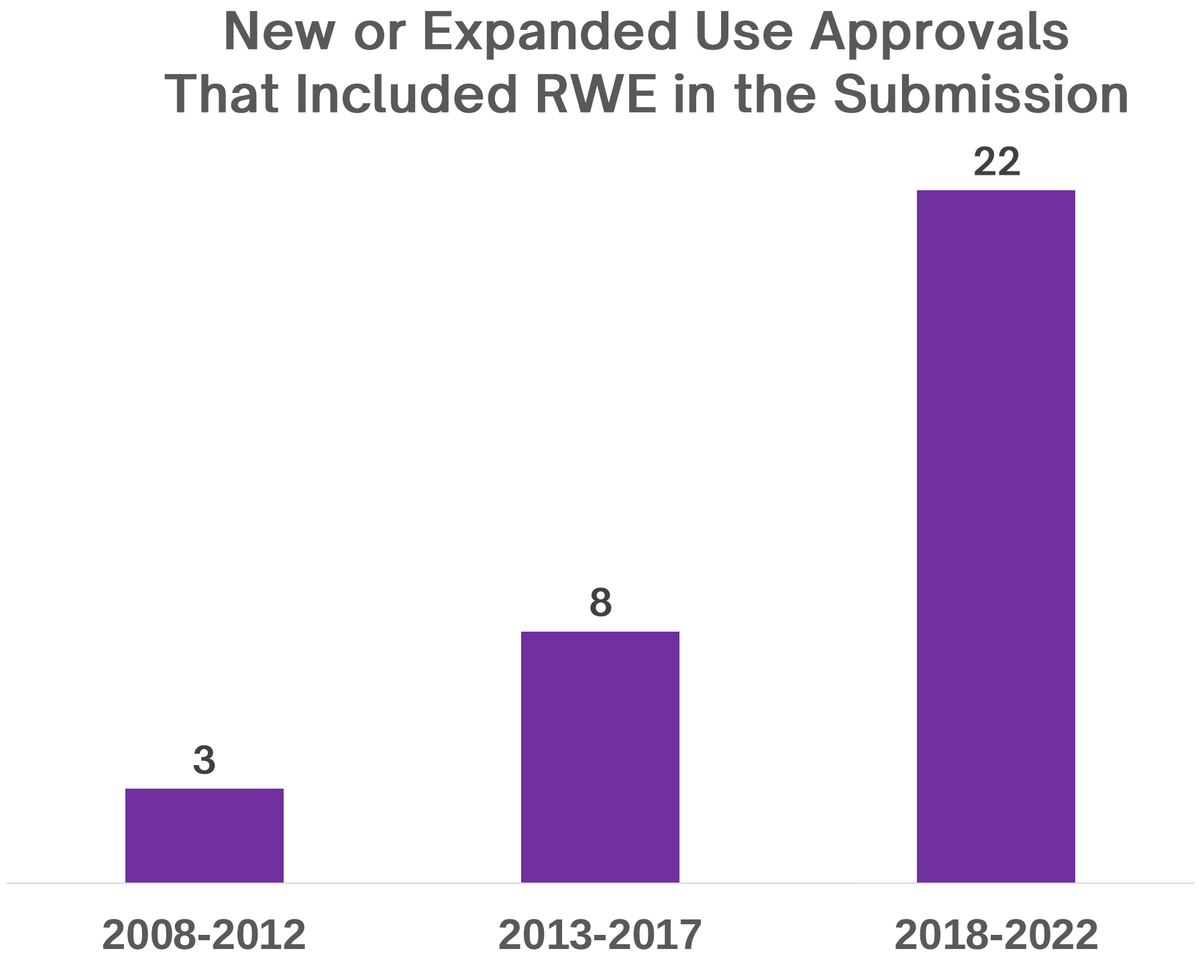
Patient and Community Orientation and Engagement

- Highest quality care
- Relevant and timely
- Accessible
- Investigative site enabled
- Improved convenience
- Representative
- Actively engaged
- Jointly ‘Owned’



Source: Tufts CSDD

Highly Leveraged Data and Analytics



- Highly accessible
- Collected continuously, faster and in real-time
- Unified
- Coordinated
- Integrated
- Predictive
- Technology and AI-Enabled

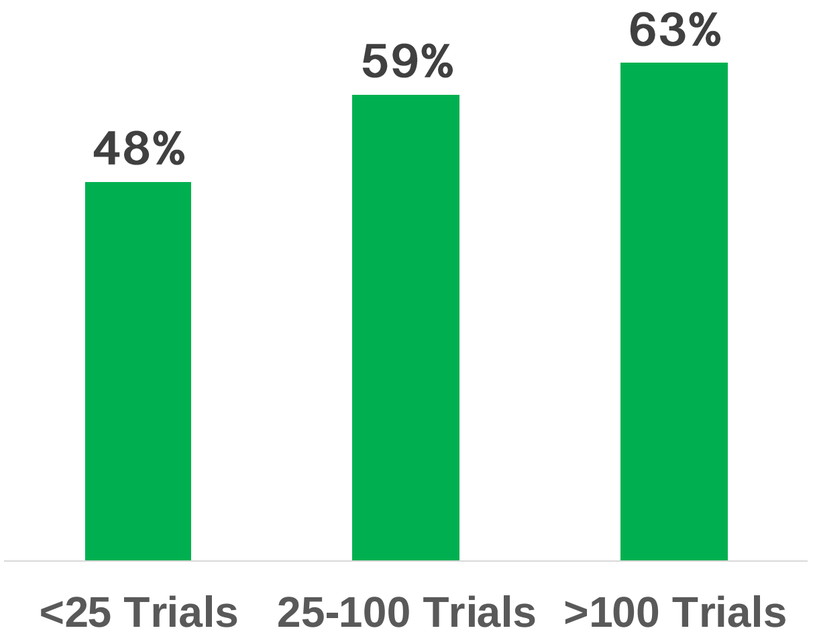
Source: IQVIA , 2023

Risk Oriented and Risk Shared

- QbD/Risk-base quality management
- Novel designs (pragmatic and umbrella trials)
- Continuous integration of clinical care/clinical research knowledge
- Shared risk with patients and payers
- Public-private cooperative studies and registries
- Open innovation and shared data from programs that have failed

Global RBQM Adoption by Company Size

(Annual Clinical Trial Volume)



Sources: Tufts CSDD, 2023; N = 125 sponsors, use of 31 RBQM components

Thank You!

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