The 2015 Avoca Report

Clinical Development Innovation

Sponsor and Provider Views on Innovation in Outsourced Clinical Development

THE AVOCA GROUP

Contents

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Research Overview

Avoca Research Overview

Introduction

Each year, The Avoca Group surveys industry executives and managers to understand trends in clinical development, with a particular focus on outsourcing dynamics and relationships between research Sponsors and Providers.

In this year's industry review, Avoca explored the topic of clinical development innovation. Specifically, we sought to understand how innovation is being utilized, from the perspective of both sponsor organizations as well as the service providers that support them, and the extent to which it is helping enhance R&D efficiency and effectiveness.

This report summarizes the key findings from our research.

Avoca Research Overview

Areas Explored in 2015

- **Perceptions of Innovative Companies**: What types of companies are driving innovation in clinical development?
- **Company Behavior/Strategy Related to Innovation:** Who is responsible for innovation and how is it funded? What types of innovative activities are being pursued, and are we progressing on goals?
- **Innovation and Provider Relationships**: How well are Sponsors and Providers collaborating on the use of innovative approaches? How does the nature of the relationship impact the ability to work together in this regard?
- **Future Outlook on Innovation**: Where is innovation most needed? Who is best positioned to drive such innovation, and how confident are we that efforts will yield meaningful results?

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

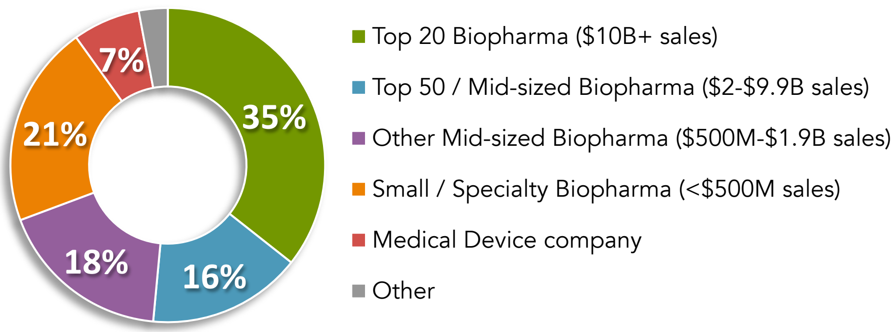
Respondent Demographics

Respondent Demographics: Sponsor

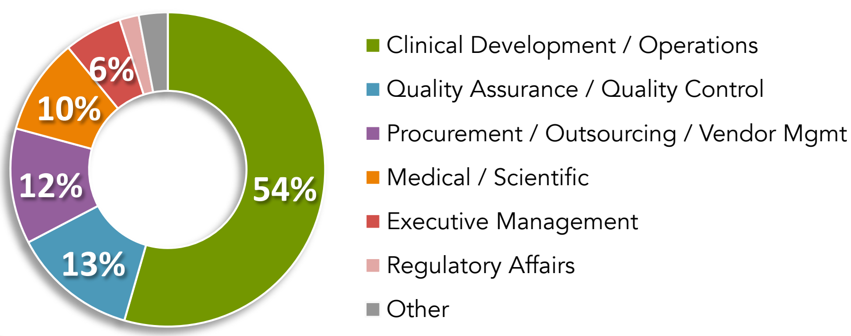
156 respondents from 85 Sponsor companies participated

83% with more than 10 years of biopharmaceutical industry experience

Company Type



Functional Area



Companies Represented

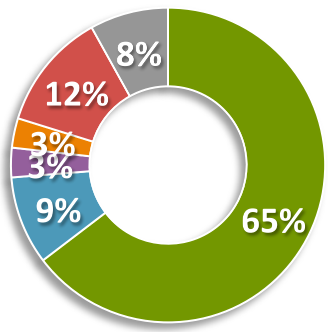
AbbVie	FibroGen	PF Labs
Achillion	Futura Medical	Pfizer
Actelion	Gennova Biopharma	Philips Healthcare
Akros	Genzyme	Pierre Fabre
Alcon	Glenmark	Plasma Surgical
Alexion	Glycotope	Purdue Pharma
Amgen	Grünenthal	Recordati
AnaMar AB	HAL Allergy	Regeneron
Arbor Pharmaceuticals	Intercept	Roche
Astellas	Italfarmaco	Genentech
AstraZeneca	Ivantis	Salix
Bavarian Nordic	Ixchelsis	Sandstone Diagnostics
Baxter	KemPharm	Sanofi
Bayer	Lundbeck	Seattle Genetics
Biological E Ltd.	MacroGenics	Serum Institute of India
Boehringer Ingelheim	Medrobotics	Shire
Boston Scientific	Menarini	Sunovion
Bristol-Myers Squibb	Merck	Takeda
Carefusion	Mitsubishi Tanabe	Tekmira
Cochlear	NeuroHealing	Tesaro
Danone	NinePoint Medical	Teva
DSPA	Novartis	The Medicines Company
Eisai	Omeros	UCB Biosciences
Eli Lilly and Company	OncoMed	United Therapeutics
EMD Serono	Onconova	Valeant
Emergent	OncoQR ML OG	Vectura
Endo	Opexa Therapeutics	ViaCyte
Endocyte	Orion Pharma	Wockhardt
Ferrer		

Respondent Demographics: Provider

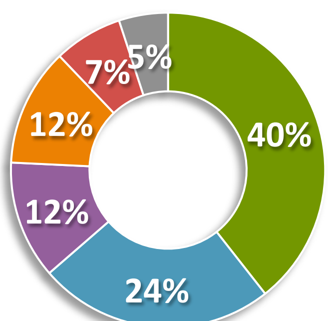
90 respondents from 61 Provider companies participated

91% with more than 10 years of biopharmaceutical industry experience

Company Type



Functional Area



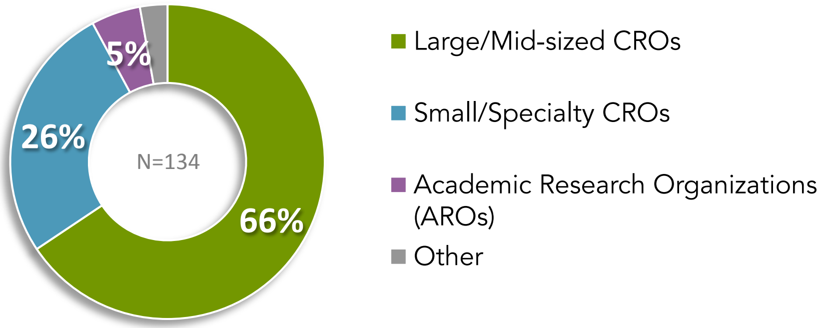
Companies Represented

Advanced Clinical	Emergent	PPD
Affairs Group Worldwide	ERT	PRA Health Sciences
Almac Clinical Technologies	ExecuPharm	Premier Research
Analgesic Solutions	Experis	Prescient
Applied Immunology	FisheClinical Services	Proscan
Aptiv Solutions	Frenova Renal Research	Quest Diagnostics
Aqix	Genelife Clinical Research	ResearchPoint
Armstrong Clinical	GlobalCare Clinical Trials	RH Bouchard & Associates
BioClinica	ICON	Rho
Biotrial	ICR	Savaan Pharma
Cardiocore	INC Research	SOLTI
Chiltern	inSeption Group, LLC	Syncro Clinical Research
Cliantha Research	Intermountain Healthcare	Target Health
Clindox Limited	inVentiv Health	Theorem Clinical Research
Clinical Excellence Group	Life Sciences	Therapeutics, Inc.
Clinically Connected	New England IRB	TKL Research
Clinlogix	PAREXEL	University Medical Research
CRF Health	PCG Clinical Services	Vantage BioTrials
CRN	PerkinElmer	Worldwide Clinical Trials
CROMSOURCE	PharmaLegacy Laboratories	
Datatrial	Popsi Cube	

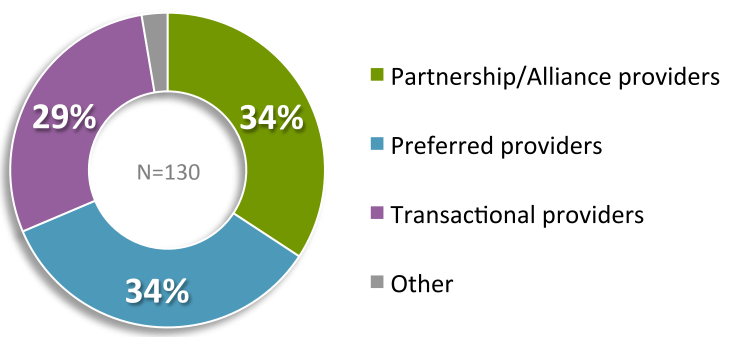
Respondent Demographics

SPONSOR
Mean %s

Spend by Provider Type

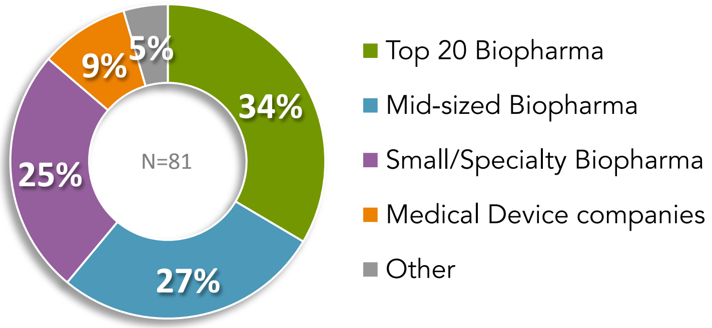


Spend by Provider Relationship

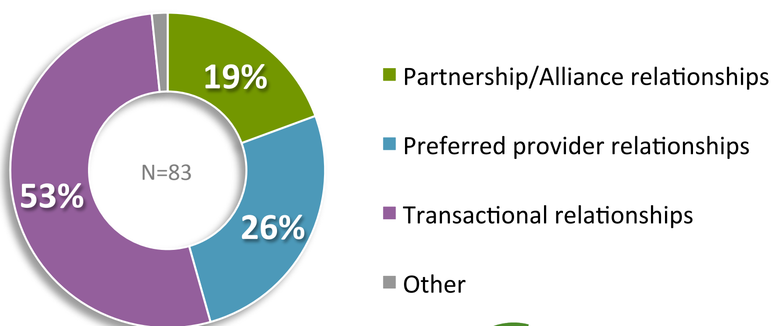


PROVIDER
Mean %s

Work by Sponsor Type



Work by Sponsor Relationship



CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

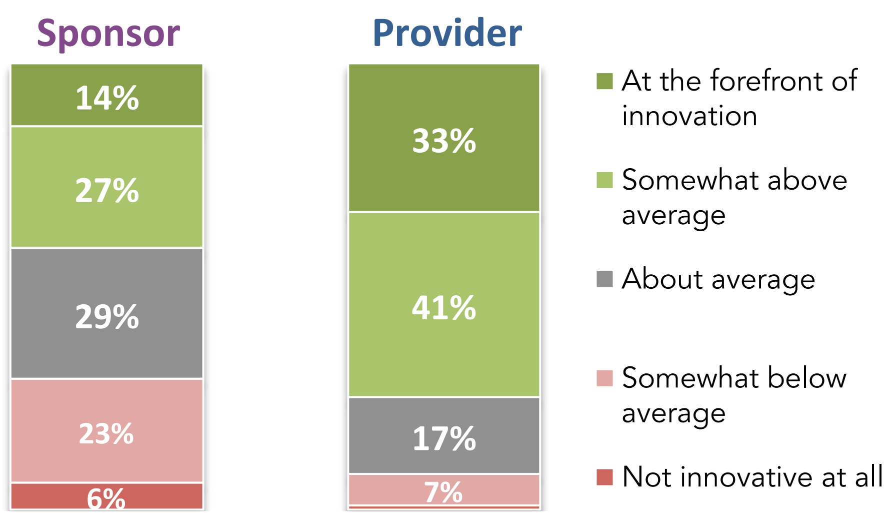
Research Findings

Innovation in Clinical Development

How innovative are we?

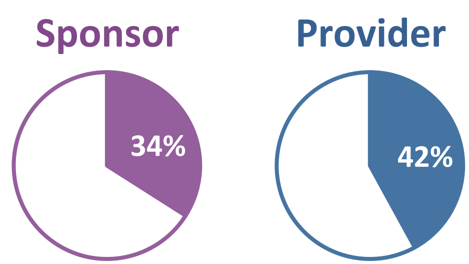
Sponsors reported using innovative approaches in about one-third of their trials, and just over 40% view their organizations as above average in innovation. Providers reported slightly higher use of innovative approaches, but nearly three-quarters consider themselves to be above average in innovation.

View of Own Organization as Innovative



% of Trials Including an Innovative Component

Mean % of 2014 Trials



EXAMPLE: "We implemented a new approach with a medical informatics vendor to contact treating MDs in almost real-time to let them know about one of our trials for recruitment purposes. We shared how we review protocol variances quarterly across programs with leaders of other clinical operations teams, and no one else had implemented something as simple and effective to manage communication around the topic."

- Specialty Pharma respondent

Sponsor N=112, 95; Provider N=69, 63

Q: *To what extent do you view your organization as innovative with respect to clinical development?* ***Q:*** *Approximately what percentage of the trials your company conducted in 2014 included some type of innovative component in the approach to clinical development?*

To what extent is clinical development innovation pursued?

Providers perceive their companies to be more committed to pursuing innovation than Sponsors along various dimensions, and there is a clear disconnect regarding the extent to which Providers are introducing innovative approaches to Sponsors.

Sponsor	My company... *% of respondents that agreed with statement*	Provider
74%	...**recognizes and adopts** innovative approaches to clinical development that are shown to be successful	92%
52%	...is **willing to try and fail** in the pursuit of innovative approaches to clinical development	70%
41%	...**invests an appropriate amount of money** and resources into innovative approaches to clinical development	72%
43%	...**has been introduced to** new innovative approaches to clinical development through its relationships with CROs / ...**has introduced** new innovative approaches to clinical development to the Sponsors we support	89%

Sponsor N=107-108; Provider N=64-66

Q: To what extent do you view your organization as innovative with respect to clinical development?

Q: Please indicate the extent to which you agree or disagree with each of the following statements:

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Which companies are leading innovation in clinical development?

When asked to identify the companies that are making the greatest strides in innovation, respondents mentioned the largest biopharma and CRO companies most frequently. Sponsors and Providers were fairly consistent in their responses

Companies Bringing Greatest Innovations to Clinical Development
Size of name represents frequency of mentions

Top 10 Biopharma Companies Mentioned

Sponsor N=73
Provider N=49

Top 10 Service Providers Mentioned

Sponsor N=71
Provider N=53

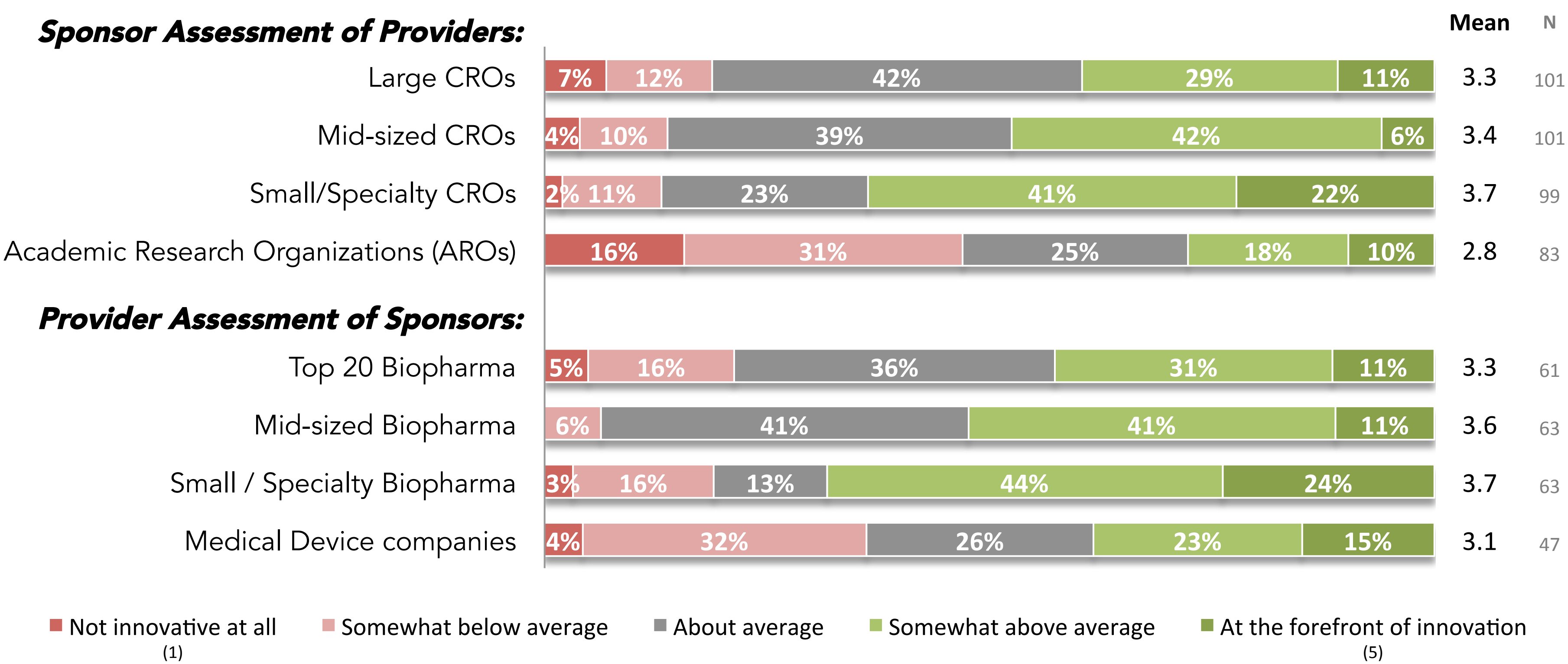
CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

***Q:** Which biopharma companies are bringing the greatest innovations to clinical development? Please list up to three.*
***Q:** Which service providers are bringing the greatest innovations to clinical development? Please list up to three.*

How are different types of organizations contributing to innovative advances?

While respondents specifically named the largest companies most frequently as contributors to innovation, when asked to evaluate the innovative abilities of various types of organizations, small/specialty companies received higher average ratings than large organizations.

Level of Innovation by Company Type



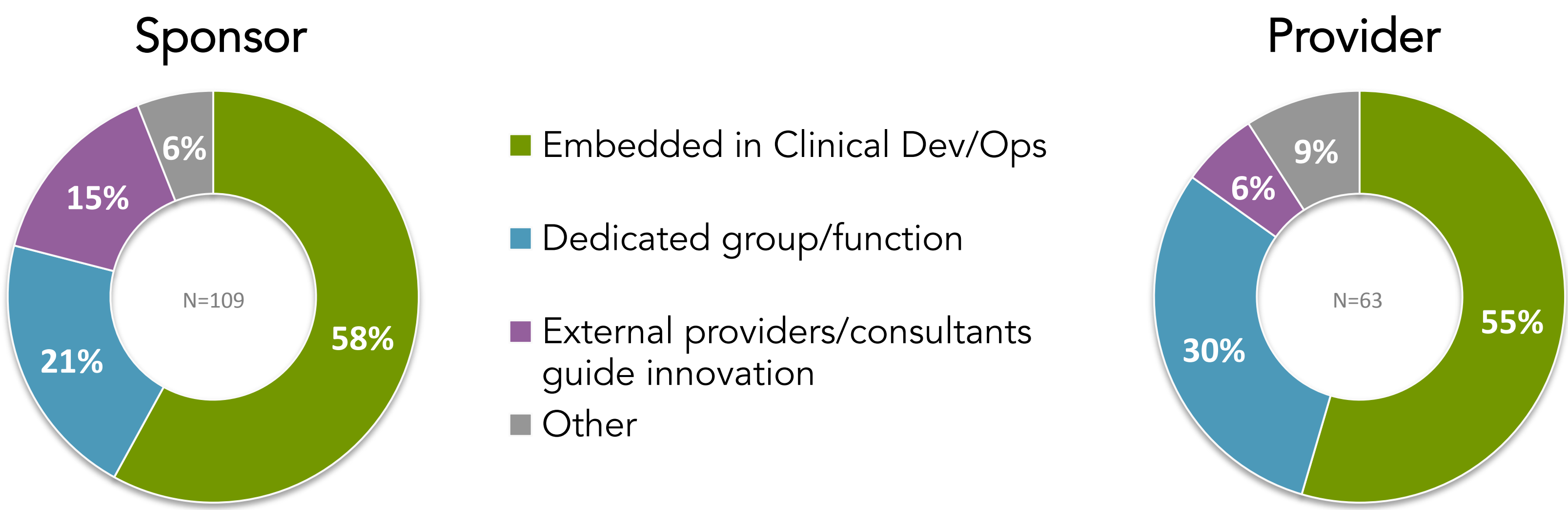
CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Q: Based on your experience, how innovative do you consider the following types of Clinical Service Providers to be?
Q: Based on your experience, how innovative do you consider the following types of Sponsors to be?

Who is responsible for innovation within Sponsor and Provider companies?

More than half of survey participants indicated that Clinical Development/Operations has responsibility for innovation within their organizations; most of the remainder reported that there is a dedicated group/function responsible for innovation at their company.

Responsibility for Clinical Development Innovation



"Implementation of innovation is a cross-functional approach and should be led by clinical development, but must be supported by all other areas, e.g. strategic management, IT, QA, etc."

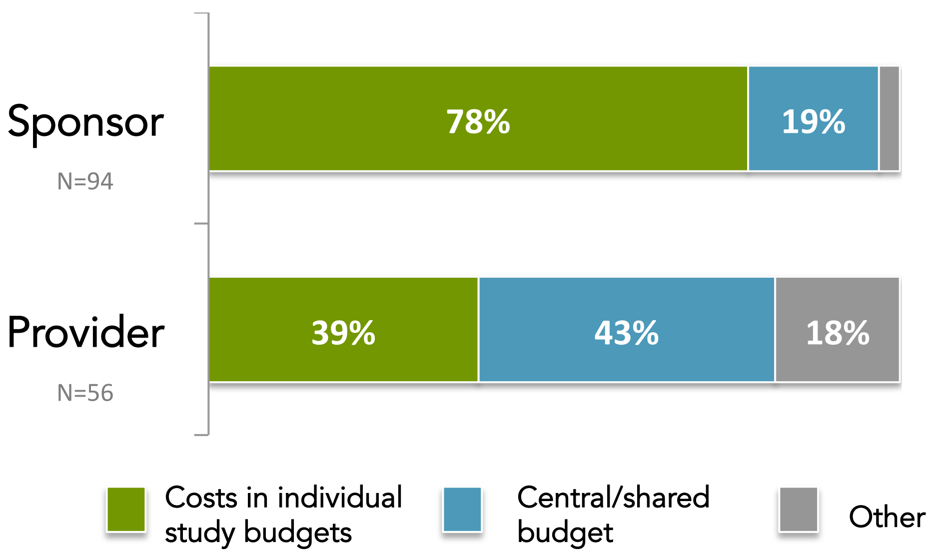
- Mid-sized Biopharma respondent

Q: *Which of the following best describes who has responsibility for innovation as it relates to clinical development within your organization?*

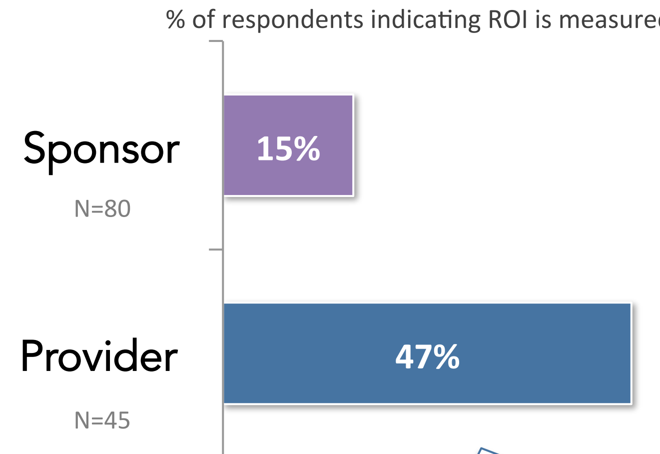
How is innovation funded and is ROI measured?

When it comes to funding innovation, three-quarters of participating Sponsors reported that costs are embedded within study budgets, while Providers are more likely to have a centralized budget. Relatively few Sponsors indicated that they have metrics to measure innovation ROI, while nearly half of Providers reported having ROI metrics.

Funding for Clinical Development Innovation



Measurement of ROI Associated with Innovation



"We have measured data query and change rates, which affect both quality and speed, and the associated costs of cleaning data. We also have figures that show how significantly reducing on-site monitoring affects cost."

- CRO respondent

Q: *Please indicate which statement best reflects how innovative clinical development approaches are typically funded at your organization.* ***Q:*** *Does your company currently have any metrics to measure the ROI associated with innovative approaches to clinical development?*

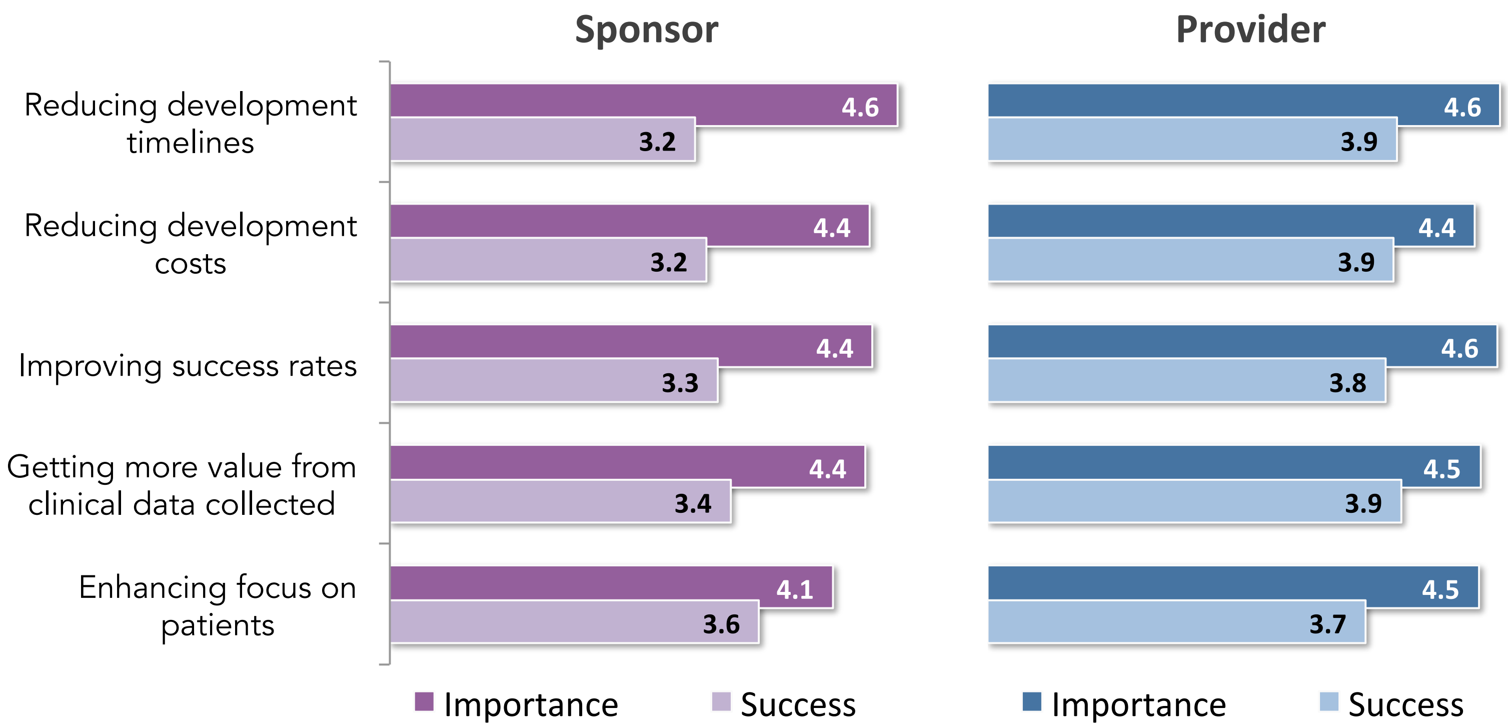
CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

What are the goals associated with innovation and are they being achieved?

Both Sponsors and Providers confirmed that various goals are important in their pursuit of innovative approaches to clinical development. In general, Providers view their companies as more successful in achieving these goals than Sponsors.

Importance and Success of Goals/Benefits of Innovative Approaches

Mean ratings on scale of 1 "Not at all Important/Successful" to 5 "Extremely Important/Successful"



Sponsor N=104-115; Provider N=64-71

***Q:** How important are each of the following goals/benefits in driving your company to pursue innovative approaches to clinical development?* ***Q:** How successful has your company been in achieving goals or recognizing benefits in each area below due to innovative approaches to clinical development?*

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

What are the primary barriers to innovation?

Sponsors and Providers are well aligned on what they consider to be the main barriers to innovation in clinical development, namely, risk aversion, company culture, and the potential cost of new approaches.

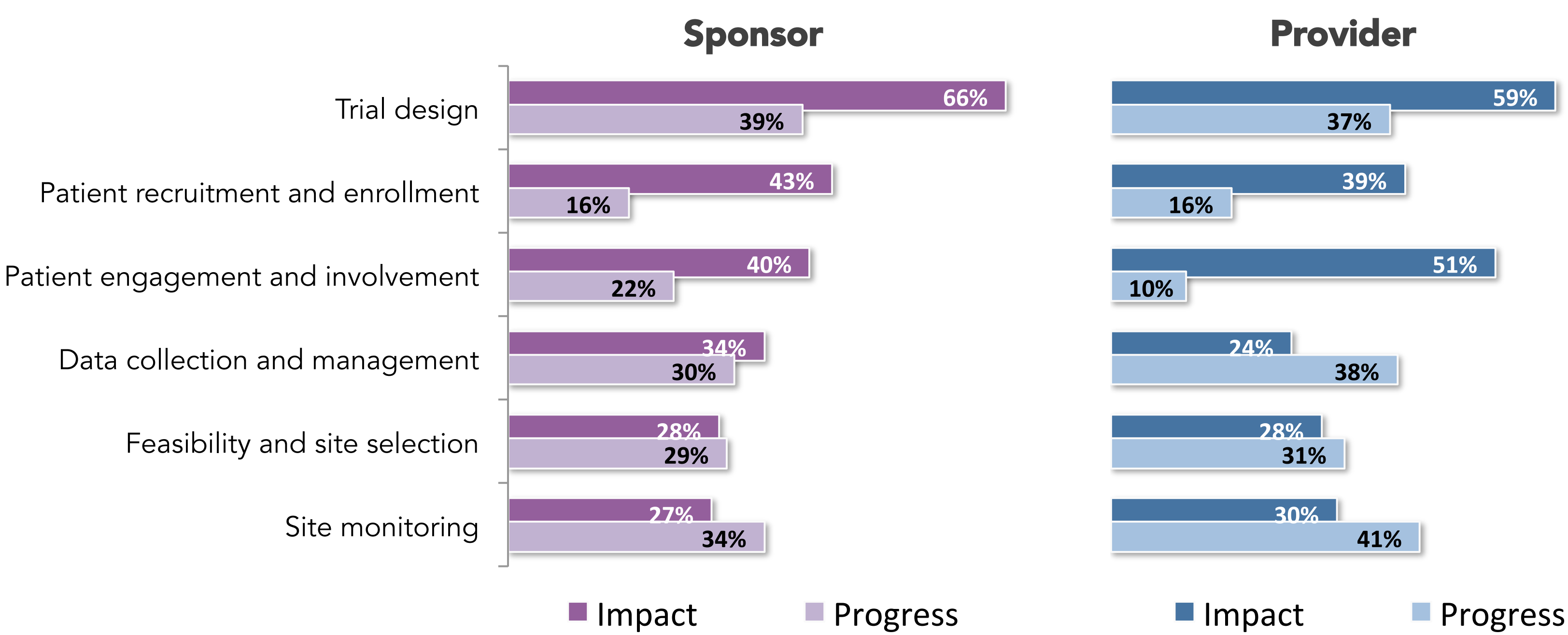
Sponsor	Provider
"(1) Mindset of employees and management, and (2) budgetary constraints – unless there is hard data showing cost savings or time savings."	"The company as a whole has a risk averse culture. In addition to this, management is financially focused."
"Decision makers would rather stick to conservative measures than to take the risk to spend money on new innovative approaches. Often decision making takes too long to allow selected measures to show an effect."	"Internally we face the same challenges as our sponsors – we need to be able to justify the investments and show potential ROI."
"Anything innovative (process, tool, etc.) that doesn't have a proven track record is less likely to be implemented until there is proof of success."	"Obtaining sponsor approval for the roll out of new approaches/capabilities on projects; reluctance to be the first project."

Q: Thinking about the company you work for, what would you say are the primary internal barriers to innovation in clinical development?

Which activities can have the greatest impact and how much progress has been made in those areas?

Trial design, patient recruitment/enrollment and patient engagement represent areas where innovation can have the greatest impact, but progress is somewhat lacking according to respondents, particularly for patient recruitment and engagement.

Top Activities Where Innovation Can Have An Impact and Where Progress Has Been Made



Less frequently selected activities included: Site engagement and management, data analysis, overall trial management and drug supply management

Sponsor N=101-119; Provider N=68-71

Q: *For the following clinical development activities, please indicate the three in which you believe innovative approaches can have the greatest impact.* ***Q:*** *For which of the following clinical development activities has your company made the most progress in utilizing innovative approaches? Please select up to three.*

What are some examples of innovative approaches that have been utilized?

When asked to describe the most innovative approach to clinical development that they have utilized or heard about, respondents most frequently offered examples involving risk-based monitoring, use of electronic health records, novel data collection and analysis techniques, and adaptive trial designs.

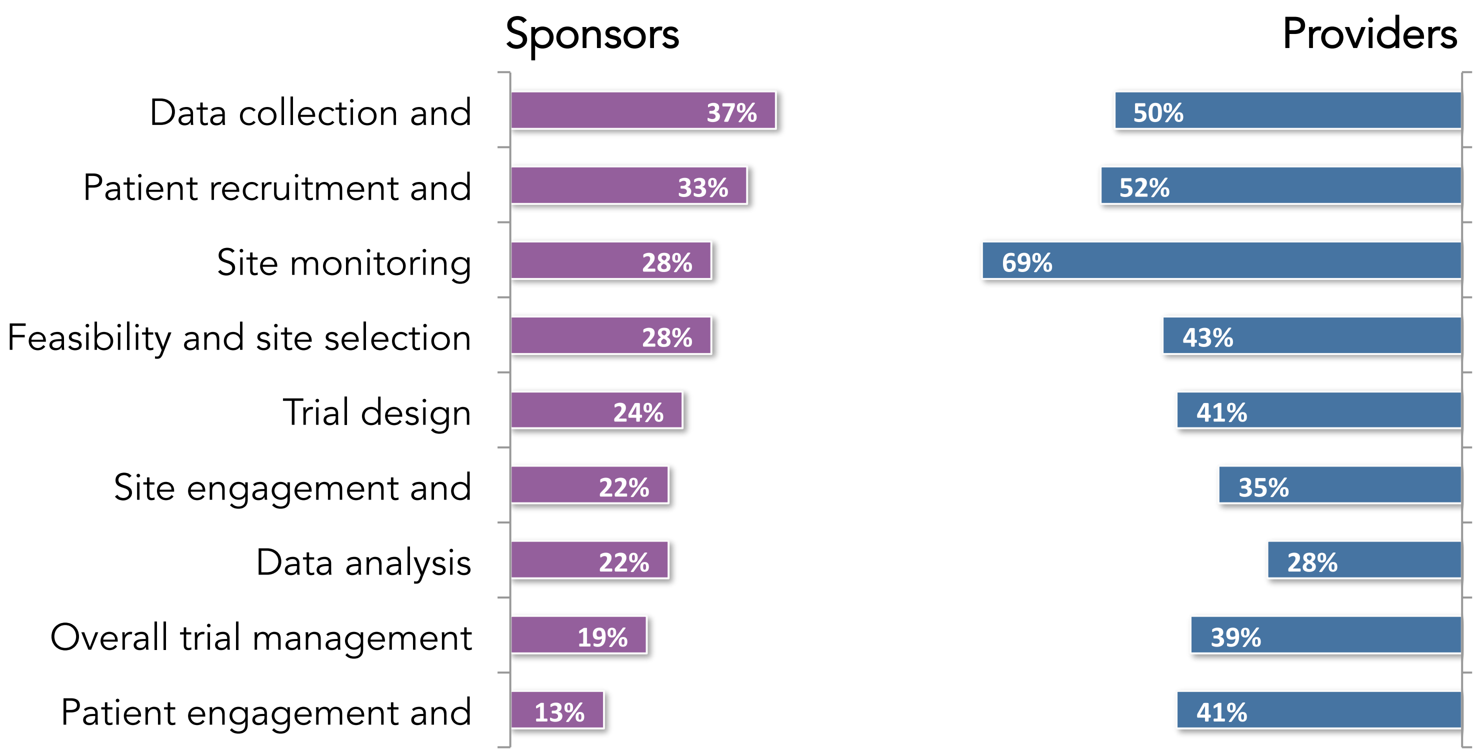
Sponsor	Provider
Trial Design	
"Import of a patient's EMR into the CRF. Remote lab capture so patients do not have to go to as many clinic visits. Use of adaptive study designs."	"Incorporating at-home visits for selected protocol tests and assessments."
Site Monitoring	
"Aiming to reduce the burden of 11% SDV and move towards risk based monitoring or targeted monitoring, shaped by the risk assessment of each study."	"Building a central monitoring hub for a key client to drive down monitoring costs and enhance productivity and quality."
Data Collection & Management	
"Electronic data capture enabling effective linking/loading of all related clinical data including SAE reporting, IxRT data, and lab data, etc."	"Because sites enter most of our study data in real-time, we look at the data every day. This, coupled with real-time edit checks at time of entry, yield better quality data, and faster time to decision-making."
Feasibility & Site Selection	
"Dedicated resources at the country level to do investigator landscaping and collate 'Voice of Site/Patient.'"	"Using data on site performance from thousands of trials, the company has created a technology enabled service to enable sponsors to select sites for future trials based upon past performance."

Q: What is the most innovative idea or approach you've heard about related to clinical drug development? Q: For each of the development activities you selected, please provide a specific example of the innovative approach(es) your company has utilized.

Which activities are Sponsors requesting and how are Providers performing in those areas?

While trial design and patient engagement are among the areas believed to offer the greatest potential impact, Providers are most frequently asked to use innovative approaches in site monitoring. From the Sponsor perspective, Providers are not meeting their innovation needs very well, particularly with respect to patient engagement.

Areas in which Providers Meet Needs / Sponsors Request Use of Innovative Approaches



Sponsor N=67; Provider N=54

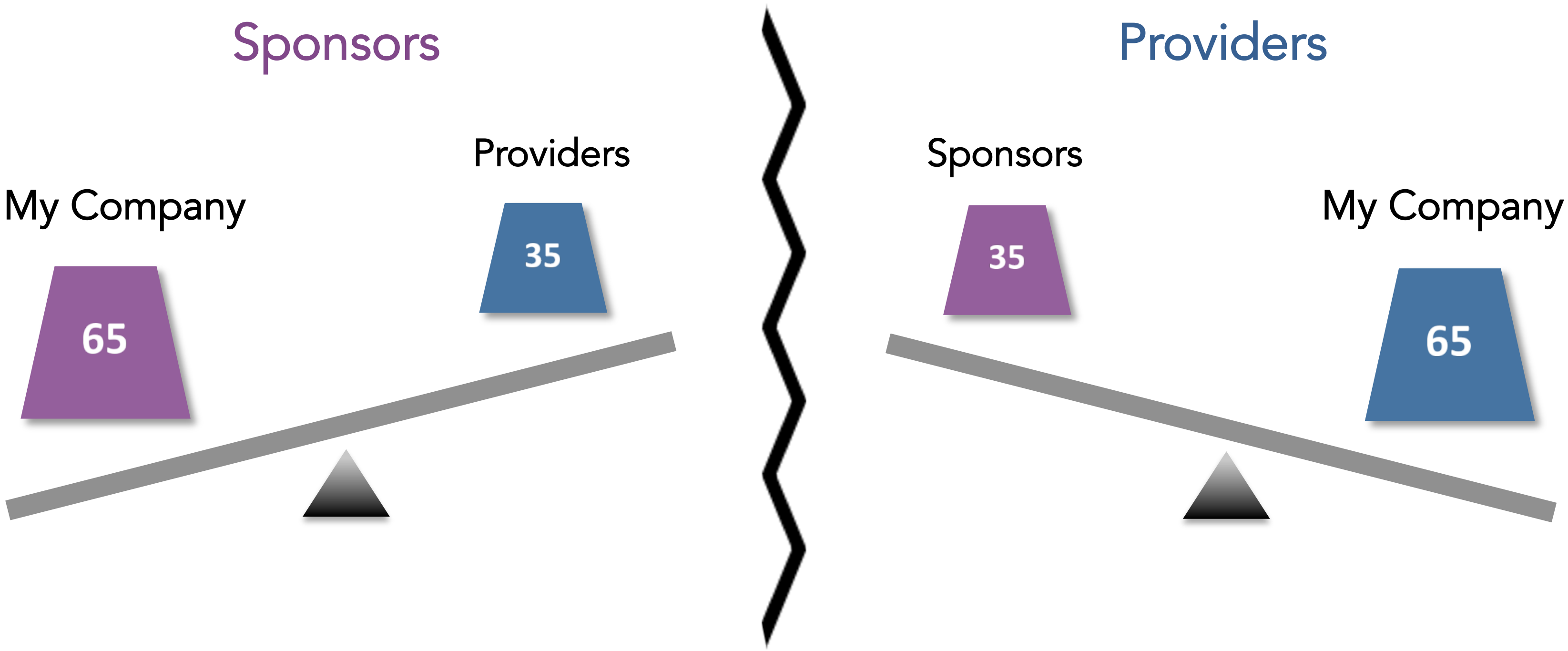
Q: *Of the following clinical development activities, in which areas are Providers meeting your needs with respect to the use of innovative approaches?* **Q:** *Of the following clinical development activities, in which areas are Sponsors requesting the use of innovative approaches?*

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Who drives innovation when Sponsors and Providers collaborate?

There is a clear disconnect regarding which party primarily drives the use of innovative approaches in outsourced clinical trials, as nearly two-thirds of both Sponsors and Providers indicated that their organization is the primary driver.

Driver of Innovation



Sponsor N=76; Provider N=49

***Q:** In your opinion, for trials your company conducts involving innovative approaches and a Clinical Service Provider, which party primarily drives the innovation? **Q:** In your opinion, for trials your company conducts involving innovative approaches, which party primarily drives the innovation? (100 point allocation)*

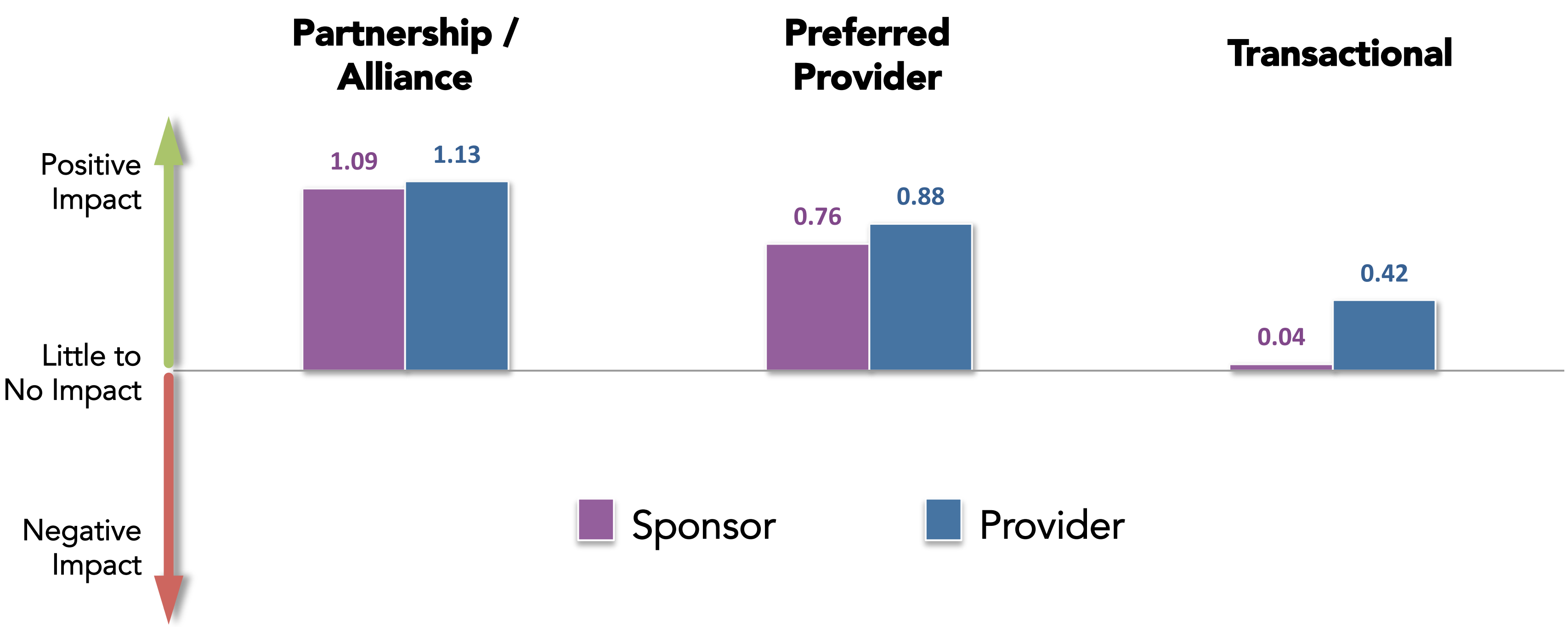
CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

How does relationship type impact the use of innovative approaches?

Overall, both Sponsors and Providers indicated that deeper relationships have a more positive impact on the use of innovative approaches to clinical development than transactional relationships.

Relationship Impact on Utilization of Innovative Approaches

Mean ratings on a scale of -2 "Strong negative impact" to +2 "Strong positive impact"



Sponsor N=89-93; Provider N=56-59

***Q:** Based on your experience, to what extent do each of the following types of relationships between Sponsors and Clinical Service Providers impact the utilization of innovative approaches?*

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

What are some examples of innovative relationships that have been formed?

Respondents offered a variety of examples when asked to describe innovative collaborations that they are familiar with, including novel approaches to contracting, organizational structure, partnering with ancillary providers, and others.

Sponsor

"The revised cost model that many recruitment firms have put into place, whereby sponsors pay based on actual patient recruitment success, on a per patient basis. This makes the recruitment firm take on a certain level of risk to the campaign they propose and execute. Essentially, this is a performance-based contract model that makes sure that the sponsor is not burdened with 100% of the cost of delayed or failed campaigns due to vendor performance."

"There is a large CRO that built a group to handle small biotechs with large trials, so the small biotech does not get lost in the competition with large pharma with many studies, and does not need or pay for the multitude of layers within the CRO structure."

Provider

"[Named IRB's] global research network. Academic Institutions that agree to become members of the network are "marketed" to Sponsors who submit studies to one of their central IRBs. Sponsors can then receive data pertaining to the institutions' metrics, e.g. study start-up times, track record in achieving enrollment goals, regulatory actions, etc."

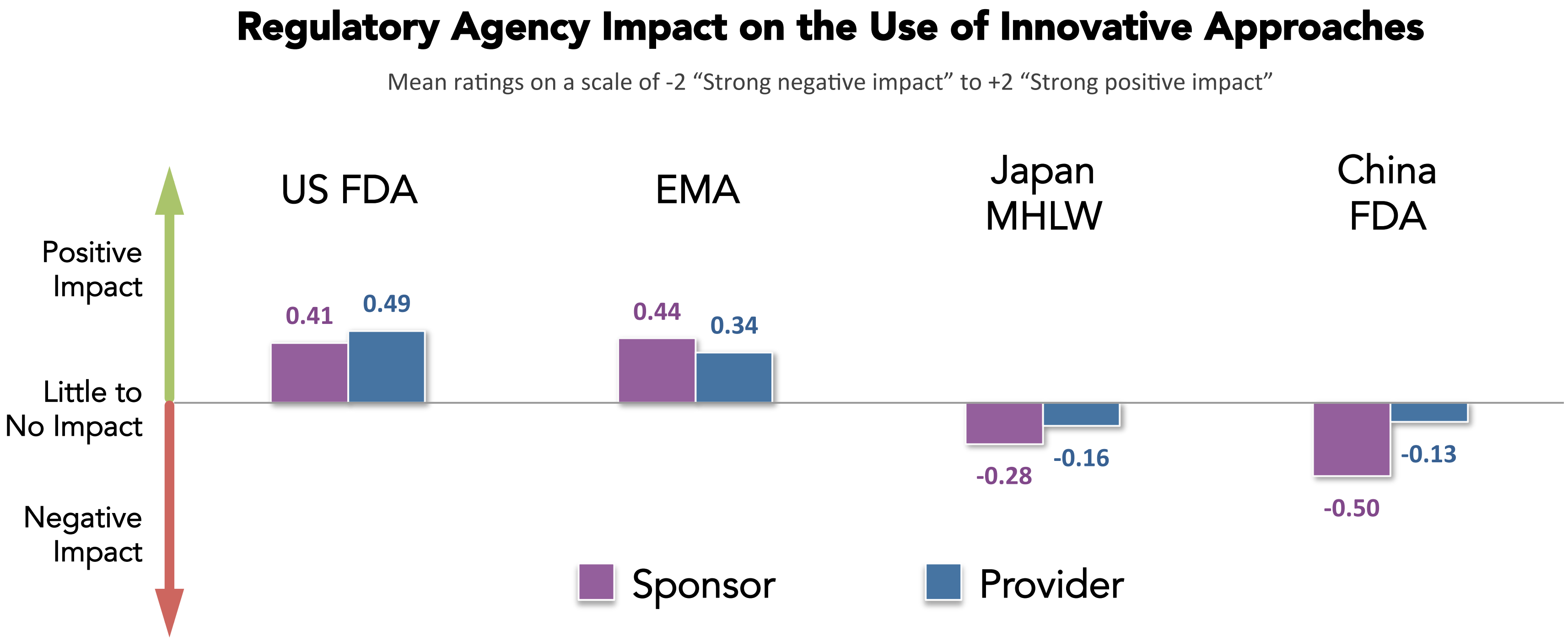
"One sponsor creating a large alliance included a central team, made up of sponsor and alliance partner staff, to drive continuous improvement. Each partner benefits from the improvements identified."

"Utilization of ambulatory care services to conduct selected protocol tests and assessments at the patient's home rather than the investigator site."

Q: Please provide an example of a relationship between a Sponsor and a Clinical Service Provider that you consider to be innovative.

What impact do regulators have on the use of innovative approaches?

The US FDA and EMA are perceived as having a positive impact on the use/adoption of innovative approaches, while the regulatory authorities in Japan and China are viewed as having a negative impact according to survey respondents.



"The Clinical Trial Transformation Task Force within the FDA has been a driving force in creating room within the regulatory framework for Sponsors to drive and/or adopt innovative approaches to development." ***- Large Biopharma respondent***

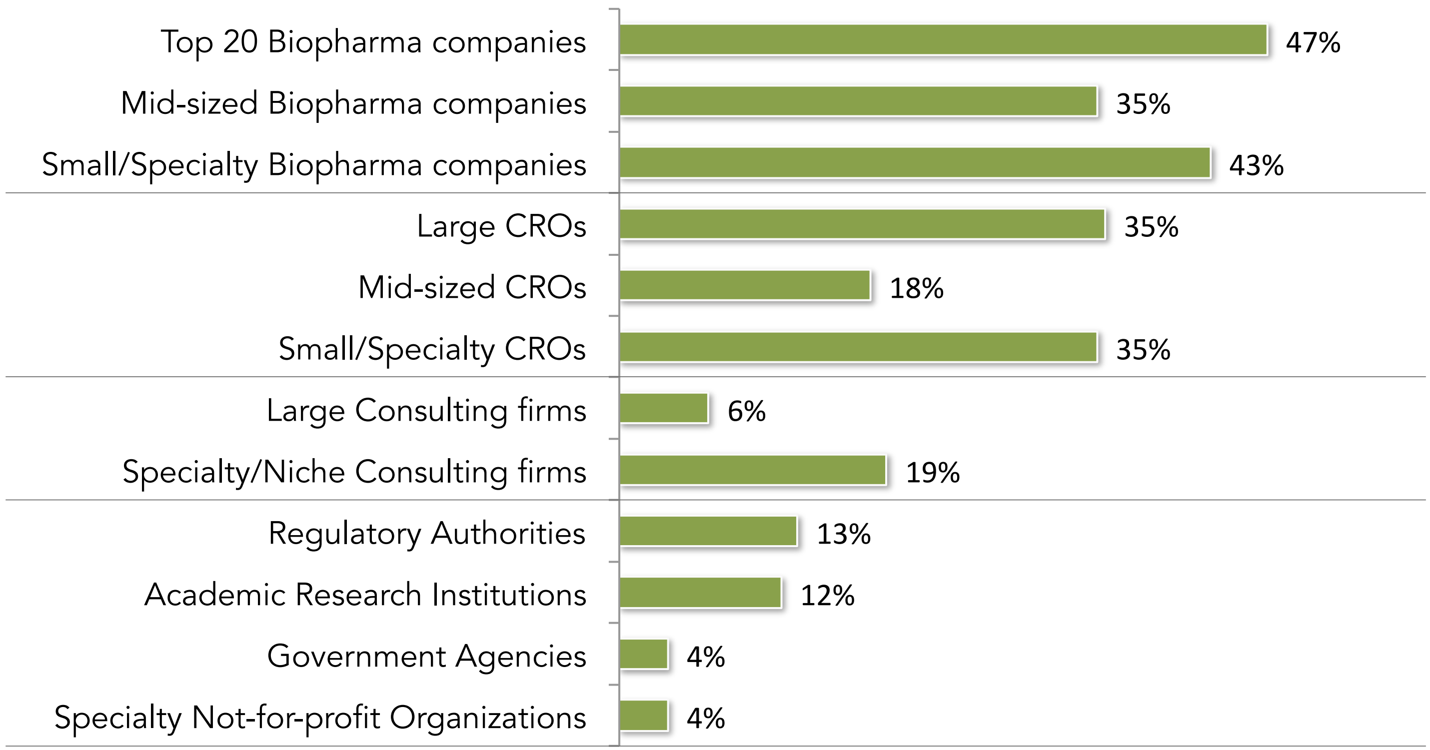
Sponsor N=64-117; Provider N=38-67

Q: *To what extent do each of the following regulatory agencies impact the use/adoption of innovative approaches to clinical development?*

What type of organizations are best positioned to drive adoption of innovative approaches?

Of the various types of organizations evaluated, respondents selected large and small biopharma companies and CROs most frequently as the ones best positioned to promote innovation in clinical development.

Organizations Best Positioned to Drive Adoption of Innovation



N=170

Q: What types of organizations do you believe are best positioned to drive adoption of innovative approaches to clinical development? Please select up to three of the following options.

Do we believe investments in innovation will pay off in the future?

Three-quarters of survey participants agreed that organizations involved in the biopharma industry will create and adopt innovative approaches that will significantly improve the way clinical development is conducted over the next five years, although less than one-third were willing to strongly agree with this prediction.

Q: Please rate your agreement with the following statement: I think the pharma industry can and will create and adopt innovative approaches that will significantly improve the way clinical development is conducted over the next 5 years.

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Summary of Findings and Key Takeaways

Summary of Findings

- Less than half of clinical trials conducted today incorporate some type of innovative component. **Providers consider themselves to be more innovative than Sponsors, and reported greater commitment to innovation** in terms of their investment, willingness to try new approaches, and adoption of novel approaches that are shown to be successful. **There is a large disconnect related to the extent to which Providers are introducing innovative approaches to Sponsors.**
- While respondents specifically named leading biopharma companies and CROs most frequently as contributors to innovation, when asked to evaluate the innovative abilities of various types of organizations**, small/specialty companies were perceived as more innovative than large organizations.**
- When it comes to funding innovation, most Sponsors indicated that costs are embedded within study budgets, while Providers are more likely to have a centralized budget. **Relatively few Sponsors reported having metrics to measure innovation ROI, compared to nearly half of Providers.**
- Both Sponsors and Providers confirmed that various goals are important in their pursuit of innovative development approaches (e.g., reducing development timelines and costs, improving success rates, etc.), but **Providers view their companies as more successful in achieving these goals than Sponsors.**

Summary of Findings

- **Trial design, patient recruitment/enrollment and patient engagement** represent areas where innovation can have the greatest impact, but progress appears to be somewhat lacking, particularly for patient recruitment and engagement. **From the Sponsor perspective, Providers are not meeting their innovation needs very well**, particularly with respect to patient engagement.
- There is strong alignment on the main **barriers to innovation** in clinical development, namely, **risk aversion, company culture, and the potential cost of new approaches.**
- There is a **clear disconnect regarding which party primarily drives the use of innovative approaches in outsourced clinical trials**, as nearly two-thirds of both Sponsors and Providers indicated that their organization is the primary driver.
- Both Sponsors and Providers confirmed the notion that **deeper relationships (e.g., alliances/ partnerships) have a more positive impact on the use of innovative approaches to clinical development than transactional relationships.**
- While most were not strongly committed to the idea, three-quarters of survey participants agreed that **organizations involved in the biopharma industry will create and adopt innovative approaches that will significantly improve the way clinical development is conducted over the next five years.**

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Key Takeaways

- Our research indicates that there are varying levels of commitment to innovation throughout the industry. For the companies that wish to pursue innovative approaches to clinical development, Avoca recommends **conducting a strategic review of potential collaborators** (suppliers, customers, others; existing relationships and those outside of the company's network) to determine **which organizations are a best fit in terms of innovation partners.**
- When pursuing collaborative innovation, companies must initially ensure alignment on goals, then **map specific activities to prioritized goals and determine how each party is expected to contribute**. This should clarify ownership and promote progress in the areas deemed most important. Establishing methods **to measure and systematically review actual vs. planned progress is critical**, and all parties should **commit at the onset of the initiative to making quick decisions** when needed to modify focus and efforts based on real-world results.
- **Patient recruitment/enrollment and patient engagement** represent areas where innovation is believed to offer high value but progress has been limited. Across the industry, **greater collaboration in these areas among Sponsors, CROs, sites and other stakeholder organizations is needed** given the importance of patient participation to the ongoing quest to develop new medicines.

CONSULTING AND RESEARCH SERVICES
THE AVOCA GROUP

Thank you

Contact Avoca at:
(609) 252-9020
www.theavocagroup.com
info@theavocagroup.com

179 Nassau Street, Suite 3A
Princeton, NJ 08542