Avoca
THE AVOCA GROUP

The 2014 Avoca Report

"Intelligent" Approaches to Clinical Development

Executive Summary

September 2014

Contents

2014 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.

One of the recurring themes that Avoca has heard via discussions and engagements with biopharmaceutical companies and providers over the past several years relates to the trend towards utilizing more "intelligent" approaches to clinical development to enhance R&D efficiency and effectiveness. Consequently, in this year's industry review, Avoca chose to perform a comprehensive assessment of how "intelligent," data-driven approaches are being utilized in outsourced clinical development today, from the perspective of both sponsor organizations as well as the service providers that support them.

This report serves as an Executive Summary of key findings from the research.

2014 Avoca Research Overview

Areas Explored

- **Application of "Intelligent" Approaches**: Frequency of use in key areas of interest; rate of advancement in these areas over the past two years
- **Contributing Forces**: Extent to which Sponsors and Providers positively or negatively contribute to the usage of "intelligent" approaches
- **Satisfaction with "Intelligent" Approaches**: Level of satisfaction with application in key areas of interest; variability in Provider application
- **Engagement with CROs**: Early engagement of partners in protocol and development planning
- **Change Management Initiatives:** Experience with technology, training, and other implementation and change management solutions

2014 Avoca Research Overview

Definitions

Respondents were provided with the following definition of "intelligent" clinical development at the beginning of the survey:

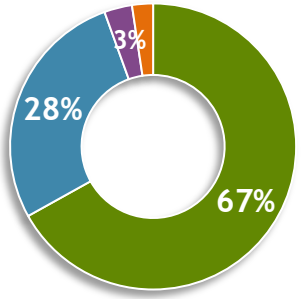
For the purposes of this survey, "intelligent" clinical development approaches are defined as those that make use of operational (e.g. performance) and/or clinical data, along with appropriate analytical techniques, in order to optimize aspects of clinical development such as protocol design, Investigator selection, patient recruitment approaches, resource allocation (e.g. risk-based monitoring), etc. For example:

- "Intelligent" approaches to overall protocol design might include adaptive study designs, i.e. those adjusted during the course of a study based on biomarker or clinical study data gathered during the study.
- "Intelligent" approaches to procedural or eligibility aspects of protocols might include examination of data from previous studies to identify procedures/criteria associated with high levels of protocol violations, cost, screen failures, etc. compared to the value of the data received.
- "Intelligent" approaches to selecting sites, regions, providers, or patient recruitment approaches might use performance databases to identify suitability for particular types of studies.
- "Intelligent" approaches to project management/oversight might include data-based identification of areas/periods of low/high risk, in order to allocate oversight resources accordingly.

Respondent Demographics: Sponsors

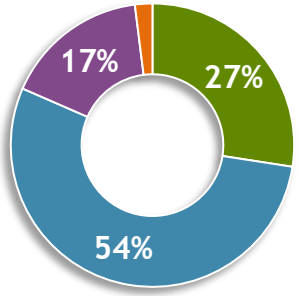
127 respondents from 83 companies; ~45% in Top 20 (by revenue)

Company Type



- Pharma
- Biotech
- Device
- Other

Role / Level



- Executive Management
- Middle Management
- Project Management
- Other

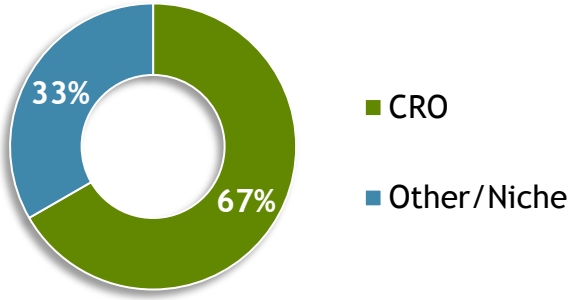
Companies Represented

Achillion Pharma	Bristol-Myers Squibb	Ipsen Biopharm	Purdue Pharma
Actelion	Cambryn Biologics	Italfarmaco	Recordati
Aeras	Cangene	Janssen R&D	Roche
Afferent Pharmaceuticals	Celator Pharmaceuticals	Johnson & Johnson	Sanofi
Alexion Pharmaceuticals	Celgene	Kowa Research Europe	Seattle Genetics
Allergan	Cerexa	Kythera Biopharmaceuticals	Shire
Almirall	Collegium Pharmaceutical	Life Science Leader	Soricimed Biopharma
Amgen	Covidien	Lundbeck	Stallergenes
Arges Pharma	Cubist	Merck	Sunovion
Array BioPharma	Dompé	Mitsubishi Pharma Europe	Synta
Astellas	Eli Lilly	MSD	Tekmira
Astex Pharmaceuticals	Endo	NanoScan Imaging	Teva Pharmaceuticals
AstraZeneca	EnVivo Pharmaceuticals	Novartis Vaccines and Diagnostics	UCB Biosciences
Bavarian Nordic	Exco InTouch	Noven Pharmaceuticals	VentiRx Pharmaceuticals
Baxter	Exelixis	Ono Pharma	Vernalis
Bayer	Genentech (member of Roche Group)	Orexigen	Vertex Pharmaceuticals
Biogen Idec	Genzyme (a Sanofi company)	Orion	Vifor Pharma
Biological E.	Grünenthal	Otsuka (OPDC)	Wockhardt
Bioniche Animal Health	Haemonetics	Pearl Therapeutics	Xenon
Boehringer Ingelheim	Helsinn Therapeutics	PF Lab	Zymogenetics (a BMS company)
Boston Scientific	HPC	Pfizer	

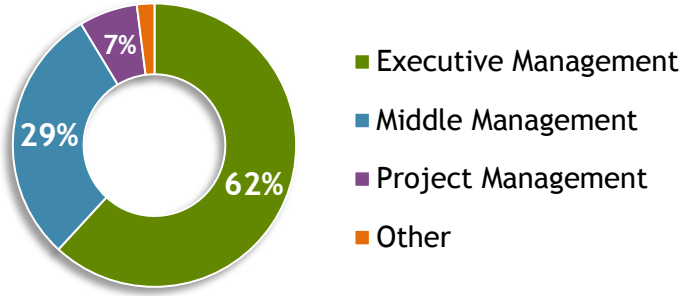
Respondent Demographics: Providers

105 respondents from 64 companies; ~64% in Top 20 (by revenue)

Company Type



Role / Level



Companies Represented

Acurian	ERT	NHS	RH Bouchard & Associates
Advanced Clinical	ExecuPharm	Novella Clinical	Schulman Associates IRB
Almac	Experis	OBiS	Sciformix
BMS (Imaging Company)	Fisher Clinical Services	OmniComm Systems	Spaulding Clinical Services
CBIO/NUDFAC-UFPE	Higginbotham Group	ORION Clinical Services	SynteractHCR
Cerafor Limited	Hugin Mugin Research	PAREXEL	Telerx
CFS Clinical	ICON	PICR	TFS Trial Form Support
Chilten	IMS Health	PlanetConnect	Theorem Clinical Research
ClinAudits	INC Research	Popsi Cube	Therapeutics, Inc.
ConcepTrial	inSeption Group	PPD	TKL Research
Consumer Product Testing Company	Interlab	PRA	TranScrip Partners
Covance	Intrinsic Imaging	ProTrials Research	UL EduNeering
CRF Health	inVentiv Health	PSI	Vantage BioTrials
Cromsource	IRB Services	QPS Holdings	Veeva
Datatrial	Micron	Quanticate	Viracor-IBT
Eperis Clinical	Moffitt Cancer Center	Quintiles	Virtuoso

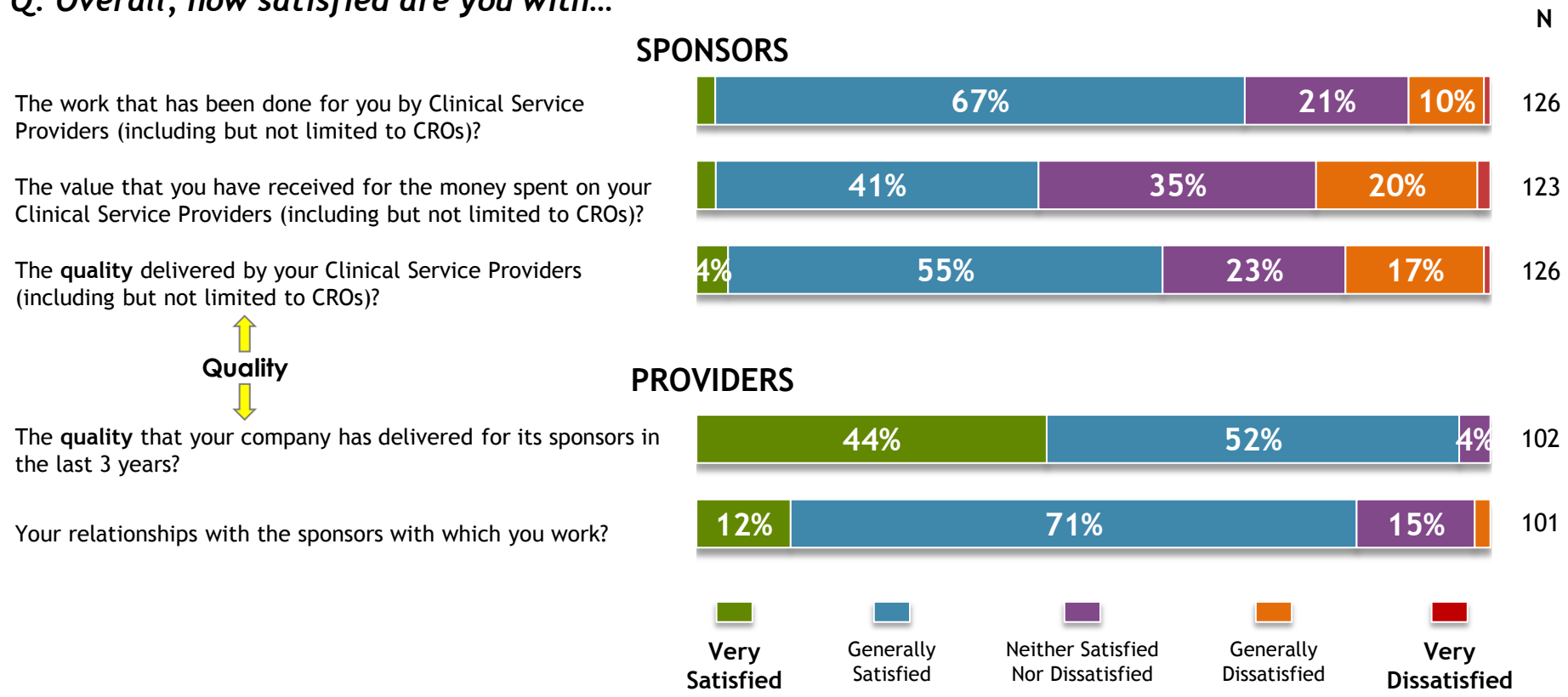
Avoca
THE AVOCA GROUP

General Perceptions of Outsourced Clinical Development

Satisfaction Levels

Respondents from Sponsor organizations generally reported lower levels of satisfaction than Providers in the respective areas evaluated. The difference in perceptions of quality has grown more pronounced, as Provider satisfaction (44% "very satisfied" in 2014 vs. 27% in 2013) has increased much more than Sponsor satisfaction (4% vs. 2%).*

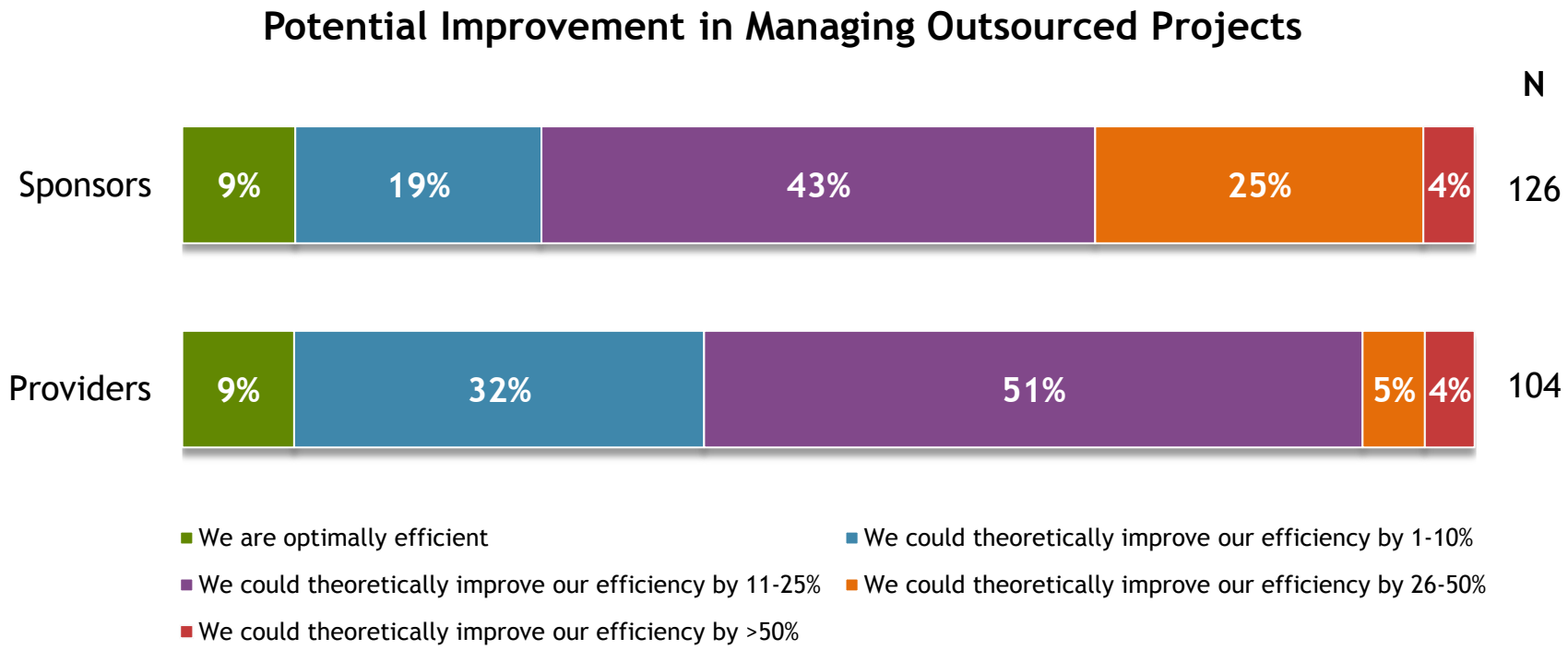
Q: Overall, how satisfied are you with…



* Refer to Avoca's 2013 Industry Report for data comparisons.

Project Management Efficiency

A greater proportion of respondents from Sponsor organizations perceive room for improvement in the efficiency with which outsourced projects are managed relative to Provider respondents. Nearly 30% of Sponsors surveyed said efficiency could be improved by more than 25%, while less than 10% of Providers reported the same.

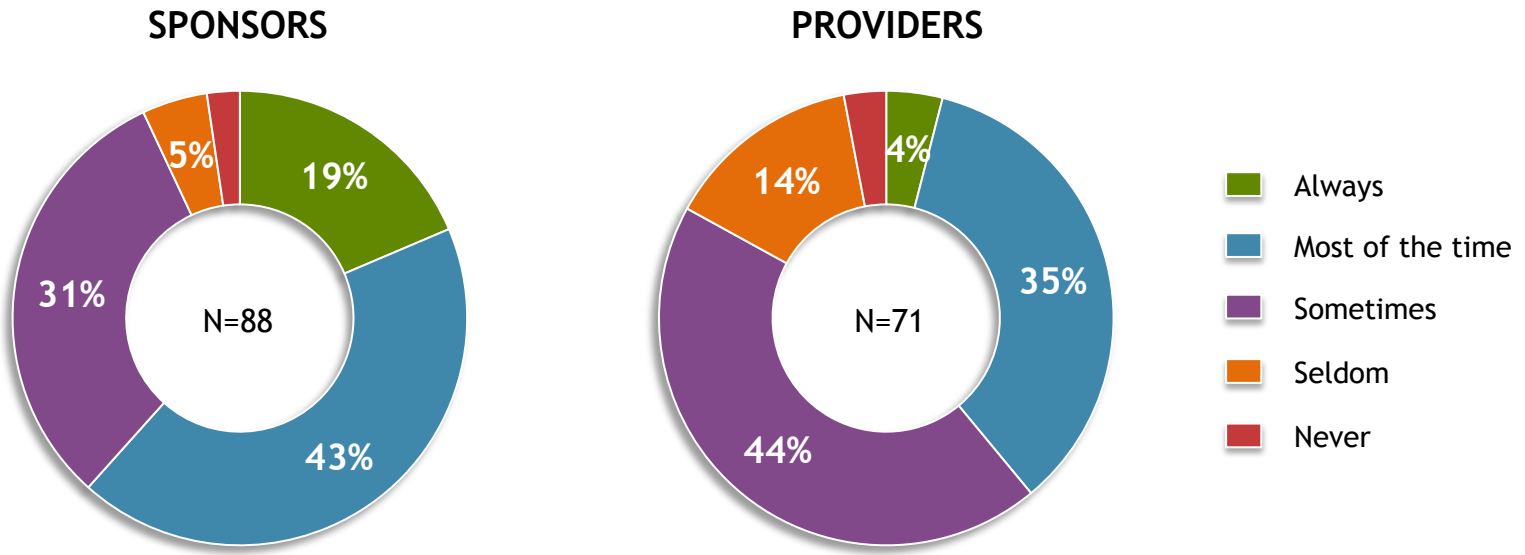


Q Sponsors: In terms of the internal resources required to manage outsourced projects effectively, how much room for improvement do you think your company currently has?
Q Providers: In terms of the resources required to manage clinical trial effectively , how much room for improvement do you think your company currently has?

Early Engagement in Clinical Trials

More than 60% of Sponsor respondents reported that they engage their CRO providers early in the process for most of the clinical trials they execute, whereas less than 40% of Provider respondents indicated that they are typically engaged early.

Early Engagement of CROs in the Clinical Trial Process

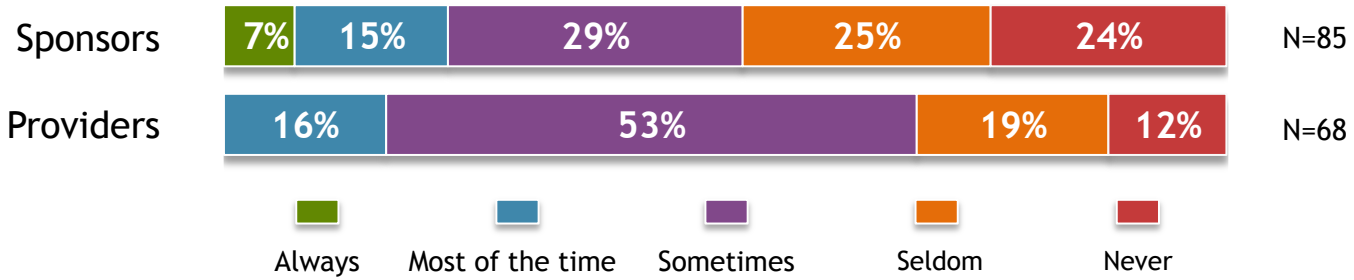


Q Sponsors: For outsourced clinical trials, how often do you engage CROs early in the clinical trial execution process, in order to leverage their experience?
Q Providers: How often do sponsors engage your company early in the clinical trial execution process, in order to leverage your company's experience?

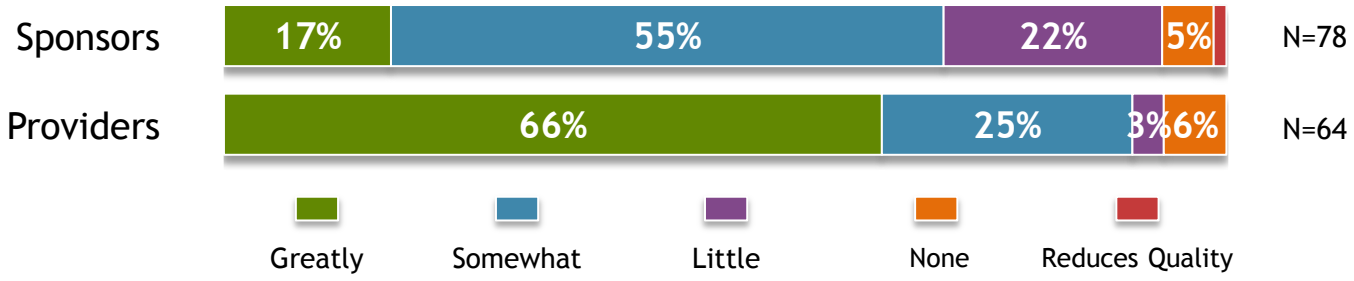
Collaboration on Protocol Design

Both Sponsor and Provider respondents had mixed views regarding the frequency of collaboration on protocol design, but there is a clear gap in terms of the extent to which Providers believe collaboration improves protocol design quality relative to the perceptions of Sponsors.

Frequency of Collaboration with CROs on Protocol Design



Extent to Which Collaboration with CROs Improves Protocol Design Quality



Q Sponsors: For outsourced clinical trials, how often do you collaborate with your CROs on protocol design? Q Providers: How often do sponsors collaborate with your company on protocol design? Q Sponsors: To what extent do you feel that collaboration with CROs on protocol design improves quality? Q Providers: To what extent do you feel that your company's collaboration with sponsors on protocol design improves quality?

Avoca
THE AVOCA GROUP

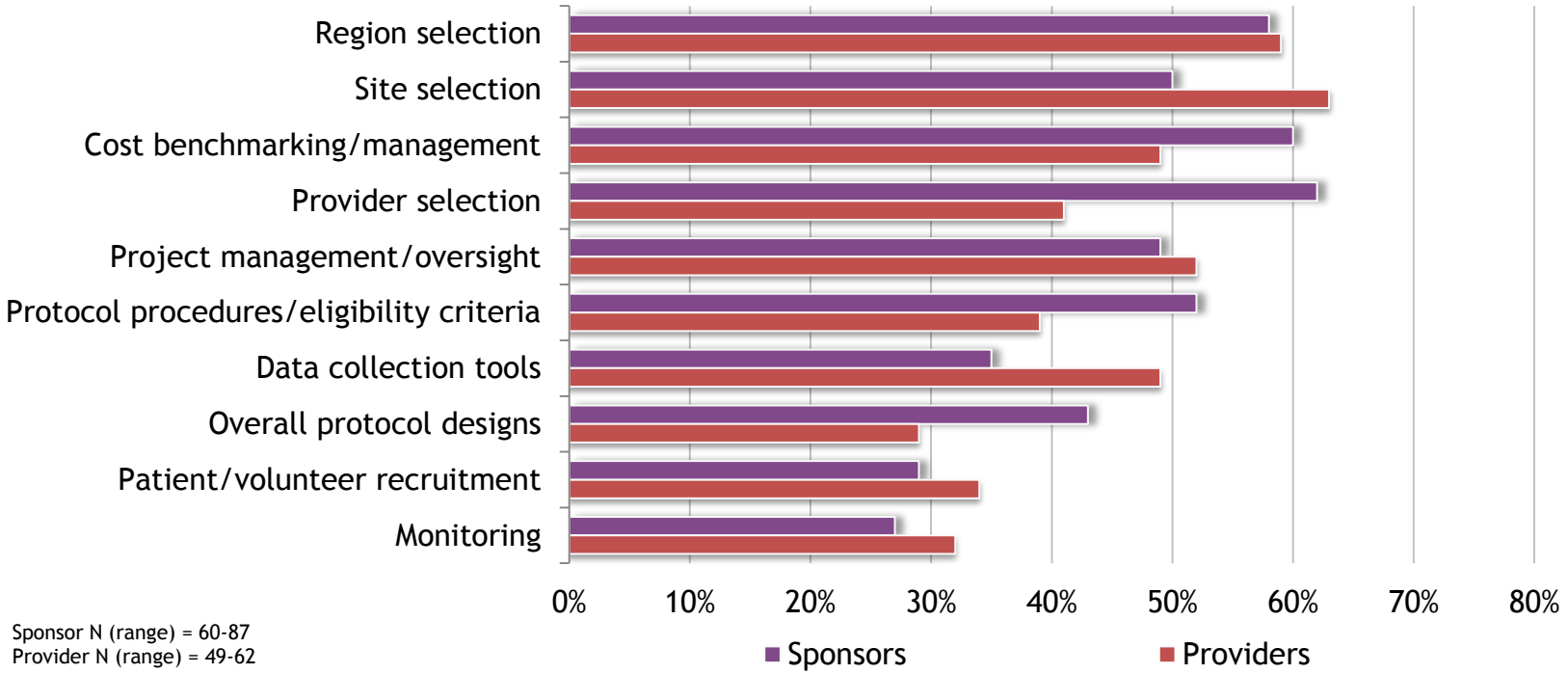
Application of "Intelligent" Approaches to Clinical Development

Use of "Intelligent" Approaches

Most respondents from both Sponsor and Provider companies reported using "intelligent" approaches to region selection and site selection for a majority of trials they conduct. Usage of these approaches for other clinical trial activities varied.

Utilization of "Intelligent" Approaches by Clinical Trial Activity

% reporting that a majority of trials conducted by their organization employ "intelligent" approaches



Sponsor N (range) = 60-87
Provider N (range) = 49-62

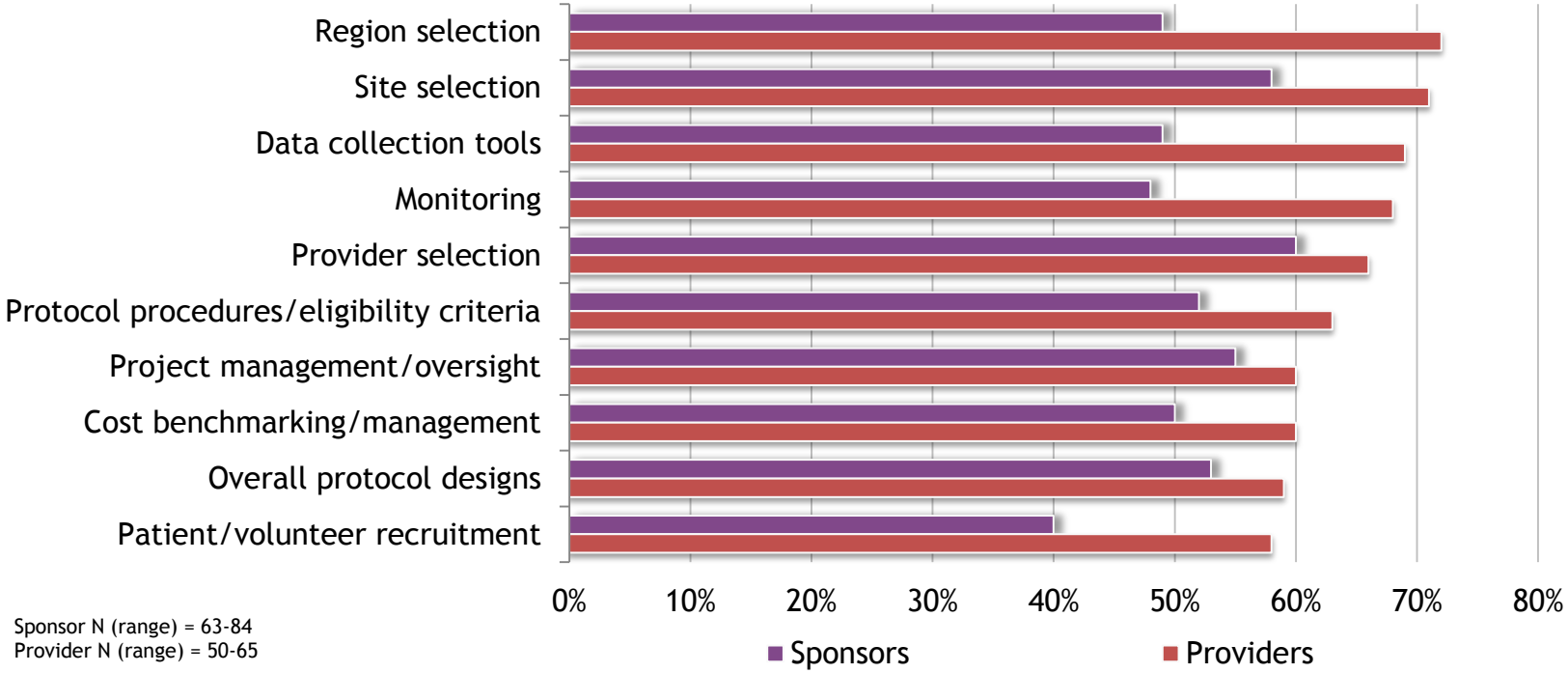
Q Sponsors: Approximately what percentage of clinical trials [conducted in-house] have employed "intelligent" (data-driven) approaches to each of the below activities?
Q Providers: For approximately what percentage of clinical trials has your company employed "intelligent" (data- driven) approaches to each of the below activities?

Advancement of "Intelligent" Approaches

A greater proportion of Provider respondents reported making at least moderate advances over the past two years in each of the clinical trial activities evaluated than Sponsor respondents. The largest gaps were associated with region selection, data collection tools and monitoring.

Advancement in the Use of "Intelligent" Approaches by Clinical Trial Activity

% reporting moderate or great advancements in the past 2 years



Sponsor N (range) = 63-84
Provider N (range) = 50-65

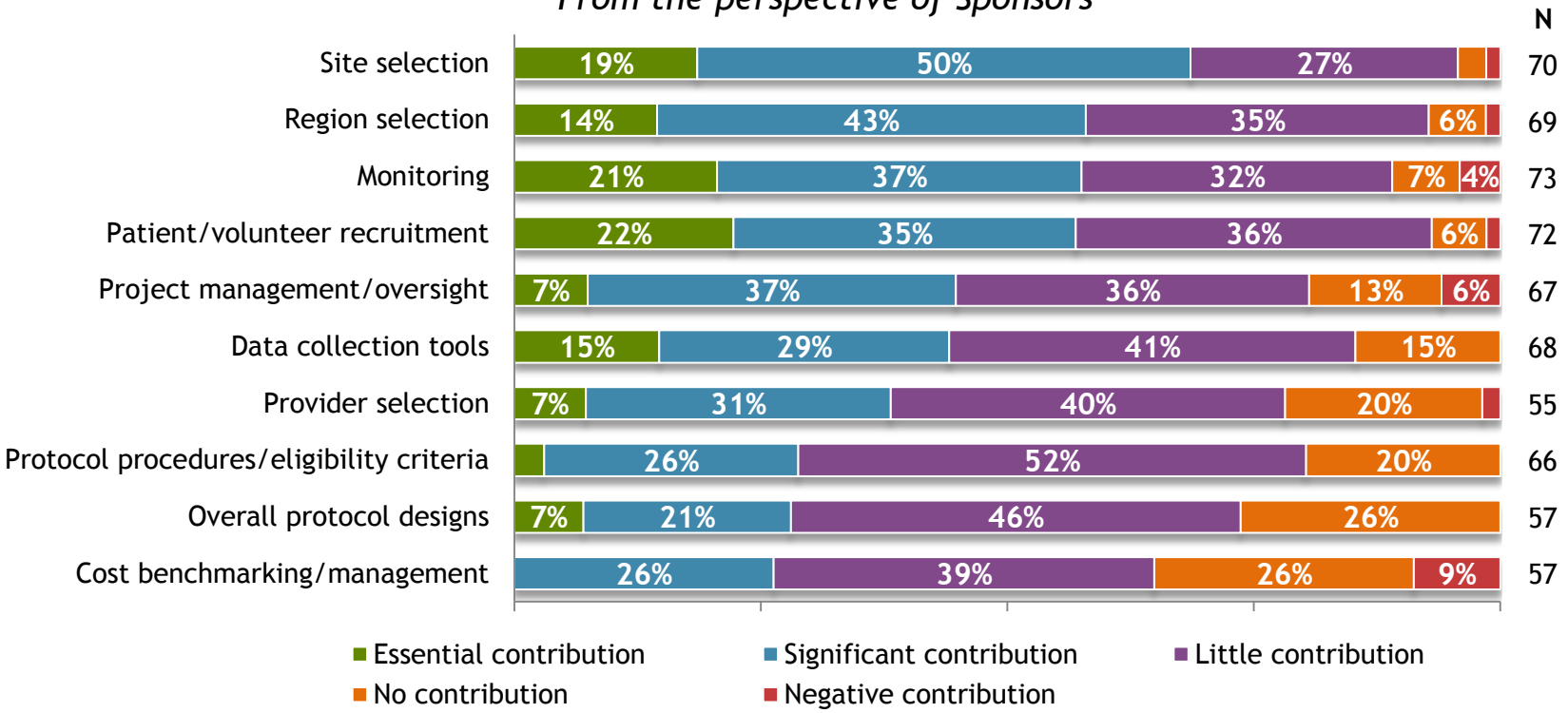
Q: Overall, how would you rate your company's advancement in the use of "intelligent" approaches to each of the below areas over the last 2 years?

Provider Contributions

A majority of Sponsors surveyed indicated that Providers are making significant or essential contributions to the use of "intelligent" approaches in four key areas: site selection, region selection, monitoring, and patient/volunteer recruitment. Sponsors perceive the smallest contributions in the area of cost benchmarking/management.

Provider Contribution to "Intelligent" Approaches by Activity

From the perspective of Sponsors



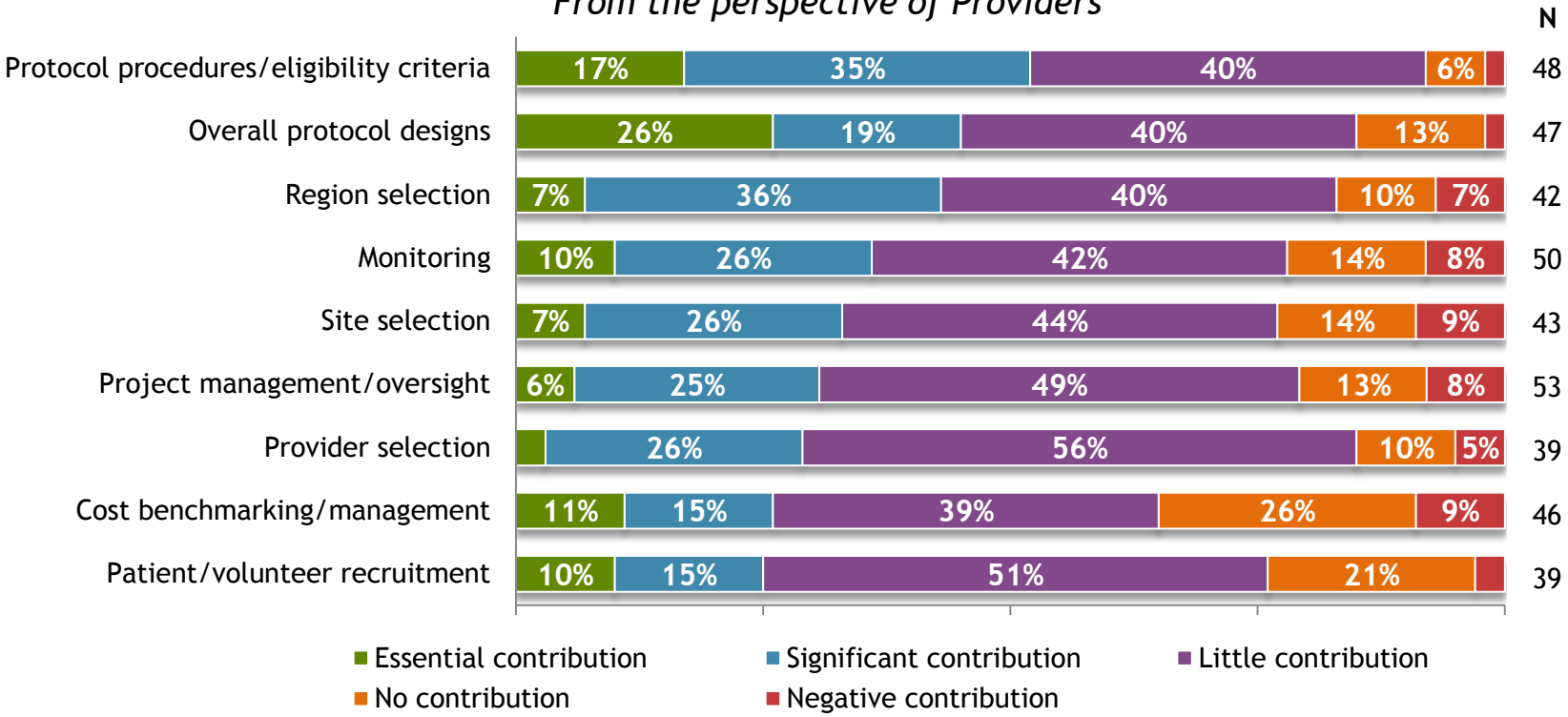
Q Sponsors: In your opinion, to what extent do your company's clinical service providers either contribute to, or detract from, your company's use of "intelligent" (data-driven) clinical development approaches for each area listed below?

Sponsor Contributions

Providers were most likely to report that Sponsors are making significant or essential contributions to protocol procedures/eligibility criteria, overall protocol design and region selection. Looking across all areas evaluated, Provider perceptions of Sponsor contributions were less pronounced than Sponsor perceptions of Provider contributions.

Sponsor Contribution to "Intelligent" Approaches by Activity

From the perspective of Providers



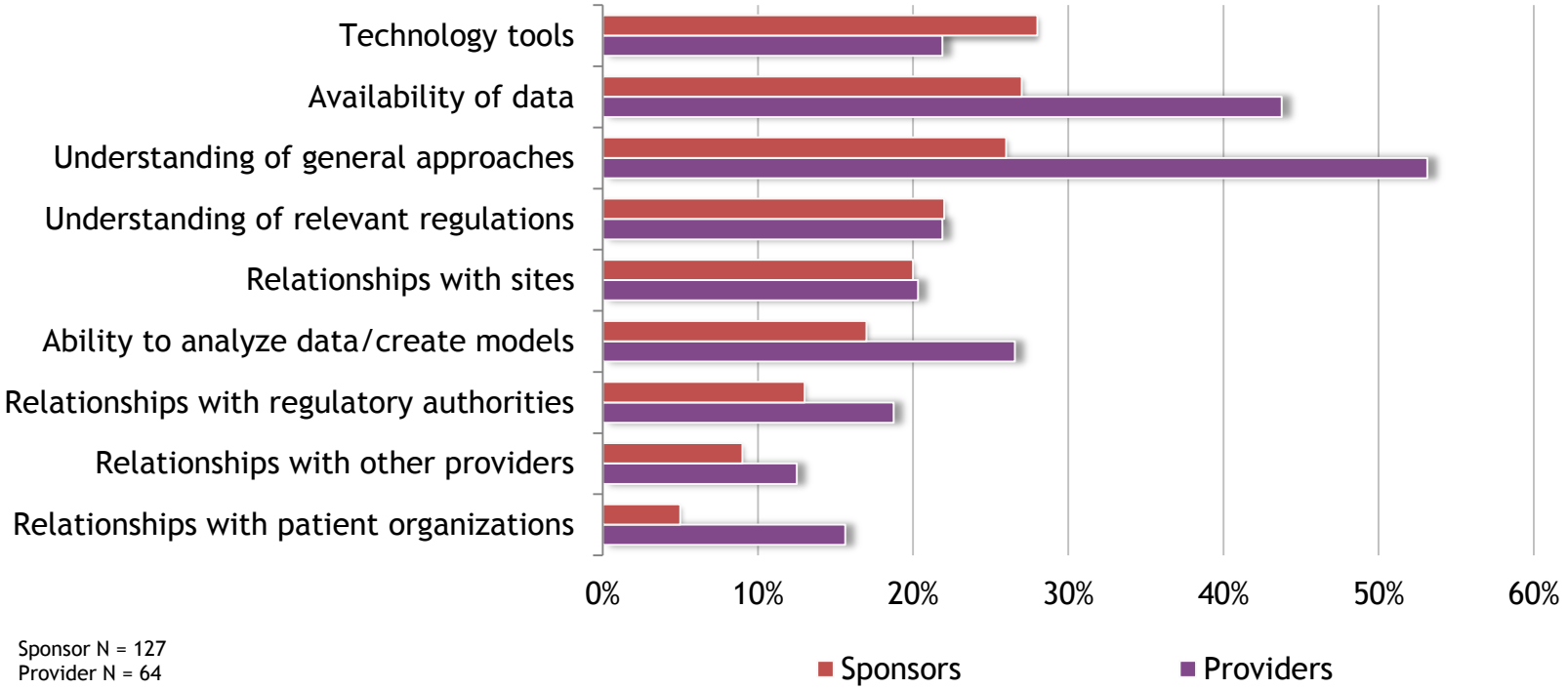
Q Providers: In your opinion, to what extent do your company's sponsor customers either contribute to, or detract from, your company's use of "intelligent" (data-driven) clinical development approaches for each area listed below?

Contributors to Adoption

A relatively large percentage of Providers acknowledged that Sponsors have contributed to their adoption of "intelligent" approaches to clinical development by helping them understand general approaches and by making data available. For Sponsors, contributions of Providers were primarily around technology and data.

Contributions to the Adoption of "Intelligent" Approaches

% reporting that the other party has contributed to their company's usage in each area



Sponsor N = 127
Provider N = 64

Q Sponsors: What have your providers contributed most to your company's adoption of "intelligent" (data-driven) approaches?
Q Providers: What have your sponsor customers contributed most to your company's use of "intelligent" (data-driven) approaches?

Contributing Forces: Open-End Themes

Q: Please describe the major contributors / impediments to your company's advancement in the use of these approaches.

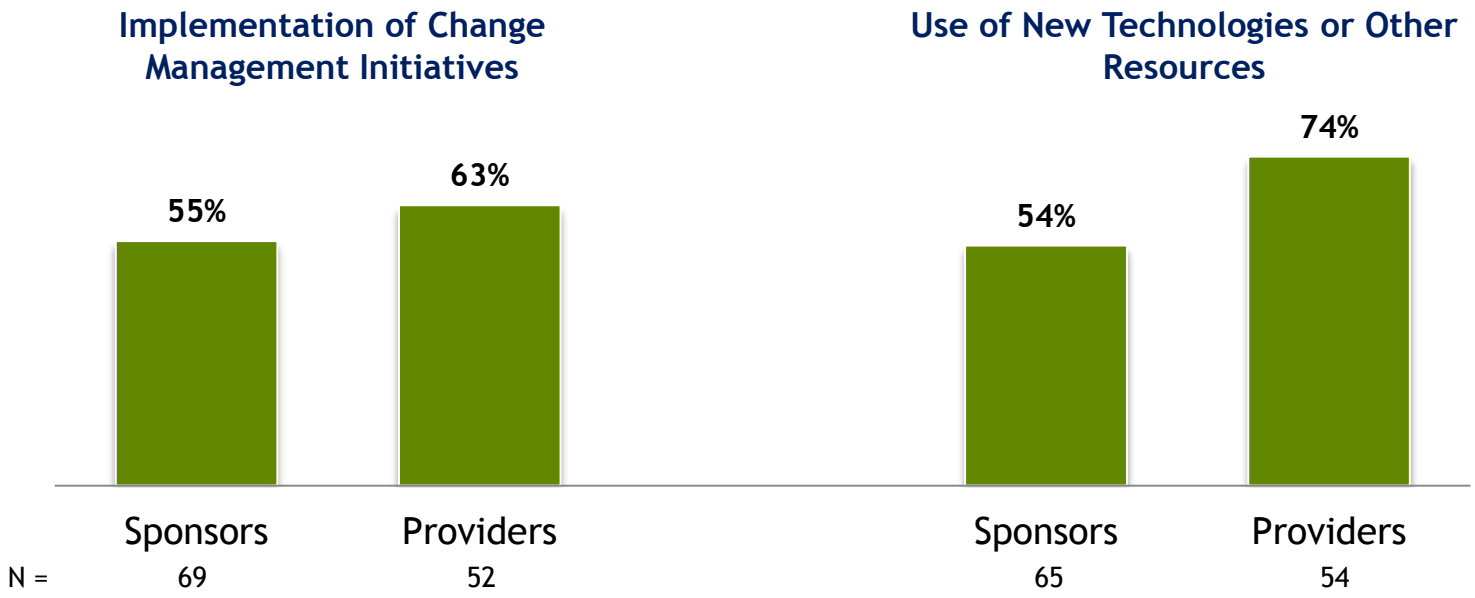
- **Internal pressures**: Pressures to increase efficiency and quality while reducing cost generally promote the use of "intelligent" approaches within companies.
- **External pressures:** Providers often reported that data-driven approaches had advanced quickly within their companies because of pressures from clients, as well as competitive pressure in general. Sponsors indicated that as examples of the use of such approaches become more prevalent in the industry, their companies/managers experience pressure to implement similar approaches.
- **Availability of data:** Use of data-driven approaches is promoted by the availability and, importantly, the aggregation of relevant data, and impeded by its absence.
- **Availability of analytical models and experience:** Likewise, the use of data-driven approaches is promoted by the availability of appropriate analytical models and experience, and impeded by its absence. Many respondents mentioned that access to expertise and experience in this area was the factor that most limited their companies' use of such approaches.
- **Understanding of regulatory perspective:** Concerns about regulatory perspectives on innovative, data-driven approaches often impact companies' willingness to "risk" their use.
- **Technology:** Technology solutions for facilitating the aggregation, analysis, and interpretation of data, particularly in a dynamic fashion, are not available to all companies.
- **Resource availability:** The use of data-driven approaches can require increased resources during the early planning and start-up stages of projects, when resources may already be limited, particularly in smaller companies.
- **Effective change management:** Like any other novel approach, the use of data-driven approaches is promoted by the availability and utilization of effective approaches to change management (e.g., training, messaging, etc.) and impeded by lack thereof.

Drivers of Increased Usage

A slightly greater percentage of Provider than Sponsor respondents reported having implemented change management initiatives to accelerate the adoption of "intelligent" approaches to clinical development, and a much greater percentage of Providers reported using new technologies in that capacity.

Methods of Facilitating Use of "Intelligent" Approaches to Clinical Development

% of respondents answering "yes"



Q: Has your company implemented any specific change management initiatives to help accelerate/improve the adoption of "intelligent" approaches to clinical trial design and execution? Q: Has your company employed any specific new technologies , consultants , etc., to facilitate the use of "intelligent" approaches to clinical trial design and execution?

Impact of Strategic Alliances

Q: What impact, if any, has the establishment of strategic alliances had on the implementation of "intelligent," data-driven approaches to clinical trial execution?

Sample Verbatim

POSITIVE

- "Strategic alliances allow for easier access to/use of data from previous studies conducted within the partnership."
- "CRO strategic partners are selected on the basis of their ability to provide this."
- "Increases trust, and hence the willingness to use innovative approaches."
- "More involvement of vendors in early stages of programs, hence more opportunity to discuss proactive data-driven approaches."
- "Cost/resource benefits of strategic partnerships have allowed more resources to be directed toward development of innovative approaches."
- "Use of partner's technology and data."
- "Ability to align processes around such approaches."

NEUTRAL / NEGATIVE

- "We have strategic alliances with CROs but the impetus for use of intelligent approaches still comes from internal staff."
- "The lack of competition has made the provider lazy with no incentive to develop or apply more intelligent or effective services."
- "Constrains alliance partners from freely partnering to leverage unique data systems and tools."

Satisfaction with Application

On average, Sponsor ratings of satisfaction with internal application of "intelligent" approaches was higher than satisfaction with Providers in nearly every area evaluated. Furthermore, a gap was observed across all areas with respect to how Sponsors view Provider performance and how Providers assessed their own performance.

Satisfaction with Application of "Intelligent" Approaches by Respondent Type

Mean Ratings. 1 = Very Dissatisfied 5 = Very Satisfied	Sponsor Ratings		Provider	Satisfaction Perception Gap
	In-House Teams	Service Providers	Self Rating	
Overall protocol designs	3.4	2.9	3.8	-0.9
Site selection	3.3	3.1	3.9	-0.8
Protocol procedures / eligibility criteria	3.4	3.0	3.7	-0.7
Cost benchmarking/management	3.3	2.5	3.2	-0.7
Patient/volunteer recruitment	3.2	3.1	3.6	-0.5
Provider selection	3.4	2.9	3.4	-0.5
Region selection	3.4	3.3	3.7	-0.4
Project management/oversight	3.4	3.0	3.4	-0.4
Data collection tools	3.4	3.3	3.7	-0.4
Monitoring	3.1	3.1	3.5	-0.4
N (range) =	49-65	34-54	37-54	

Q Sponsors: For each of your in-house teams and your clinical service providers, please rate your levels of satisfaction with their application of "intelligent" (data-driven) approaches on your projects, in each of the below areas. Q Providers: Please rate your levels of satisfaction with your company's application of "intelligent" (data-driven) approaches, in each of the areas below. Please use a scale of 1 to 5, with 1 meaning "very dissatisfied" and 5 meaning "very satisfied."

Avoca
THE AVOCA GROUP

Summary of Findings and Takeaways

Summary of Findings

- Respondents from Sponsor organizations generally reported lower levels of satisfaction than Providers in the respective areas evaluated. The difference in perceptions of quality has grown more pronounced, as Provider satisfaction (44% "very satisfied" in 2014 vs. 27% in 2013) has increased much more than Sponsor satisfaction (4% in 2014 vs. 2% in 2013).
- A greater proportion of respondents from Sponsor organizations perceive room for improvement in the efficiency with which outsourced projects are managed relative to Provider respondents. Nearly 30% of Sponsors surveyed said efficiency could be improved by more than 25%, while less than 10% of Providers reported the same.
- More than 60% of Sponsor respondents reported that they engage their CRO providers early in the process for most of the clinical trials they execute, whereas less than 40% of Provider respondents indicated that they are typically engaged early in the process.
- Both Sponsor and Provider respondents had mixed views regarding the frequency of collaboration on protocol design, but a much greater percentage of Providers than Sponsors reported believing that collaboration greatly improves protocol design quality.

Summary of Findings

- Most respondents from both Sponsor and Provider companies reported using "intelligent" approaches to region selection and site selection for a majority of trials they conduct, and close to half reported using these approaches for cost management and project management. Usage of "intelligent" approaches for other clinical trial activities varied.
- A greater proportion of Provider respondents reported making at least moderate advances over the past two years in each of the clinical trial activities evaluated than Sponsor respondents. The largest gaps were associated with region selection, data collection tools and monitoring.
- A majority of Sponsors surveyed indicated that Providers are making significant or essential contributions to the use of "intelligent" approaches in four key areas: site selection, region selection, monitoring, and patient/volunteer recruitment. Sponsors perceive the smallest contributions in the area of cost benchmarking/management.
- Providers were most likely to report that Sponsors are making significant or essential contributions to protocol procedures/eligibility criteria, overall protocol design and region selection. Looking across all areas evaluated, Provider perceptions of Sponsor contributions were less pronounced than Sponsor perceptions of Provider contributions.

Summary of Findings

- A relatively large percentage of Providers acknowledged that Sponsors have contributed to their adoption of "intelligent" approaches to clinical development by helping them understand general approaches and by making data available. For Sponsors, contributions of Providers were primarily around technology and data availability.
- A slightly greater percentage of Provider than Sponsor respondents reported having implemented change management initiatives to accelerate the adoption of "intelligent" approaches to clinical development, and a much greater percentage of Providers reported using new technologies in that capacity.
- On average, Sponsor ratings of satisfaction with internal application of "intelligent" approaches was higher than satisfaction with Providers in nearly every area evaluated. Furthermore, a gap was observed across all areas with respect to how Sponsors view Provider performance and how Providers assessed their own performance.

Key Takeaways

- There remains a gap in perceptions among Sponsors and Providers in various areas, including overall quality that is being delivered, the impact of collaborating on protocol design, and satisfaction associated with the application of data-driven approaches to clinical development. Both parties could benefit from investing additional time at the beginning of a relationship (or at the program level) using a formal, structured approach to clarify roles and expectations, and document:
  - How quality will be assessed and measured.
  - The extent to which Providers will have input on protocol design and other early program activities.
  - The tools and capabilities each party offers to support data-driven approaches to various program activities and how to optimize usage.
- While significant advancements have been made in the movement towards more "intelligent" approaches to clinical development, additional progress and consistency is needed to realize the full potential of these new approaches. Both Sponsors and Providers should develop tailored strategies to guide investment in this area with very clear priorities regarding capabilities needed in-house vs. those best fulfilled via relationships with external providers. Strategies must be designed to evolve with changing marketplace dynamics (technological, economic, regulatory, etc.).

Avoca
THE AVOCA GROUP

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

179 Nassau Street
Suite 3A
Princeton, NJ 08542