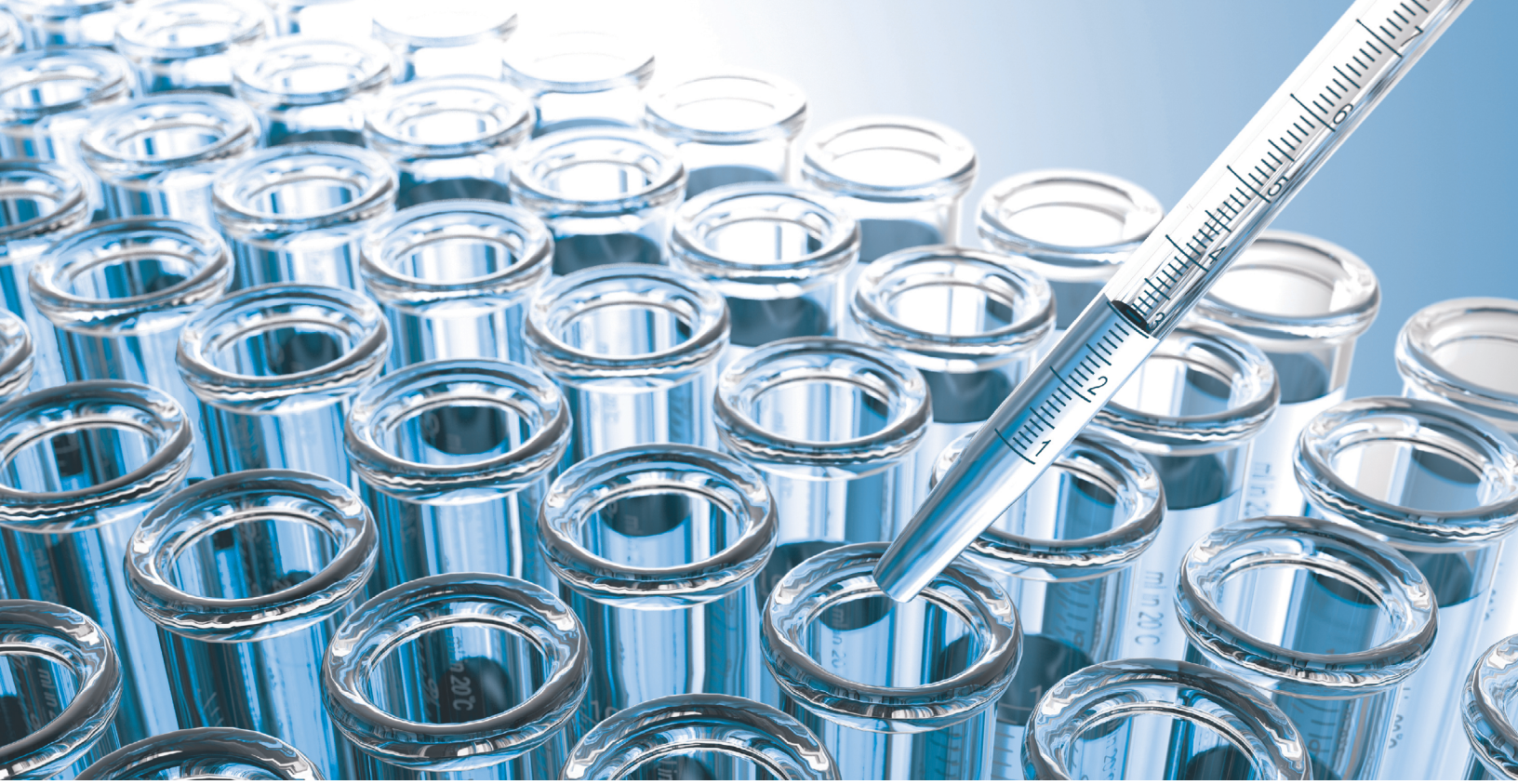

Sponsor-CRO Collaboration Study

2013

vantage partners

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Contents

Part One

About the study and participant demographics

Methodology overview

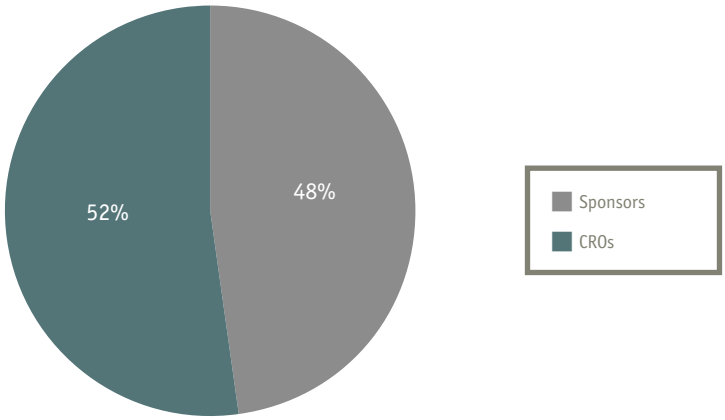
- Survey of CRO executives, as well as directors of Business Development, Clinical Operations, Data Management, Regulatory Affairs, etc., and project managers (comprising 88 individual respondents).
- Survey of Sponsor executives, as well as directors and managers from functions such as Clinical Operations, Clinical Outsourcing, Data Management, and Supply Chain (comprising 81 individual respondents).*
- Interviews were conducted with more than 20 individuals representing a cross-section of roles, across both CROs and pharmaceutical Sponsors, including multiple geographic regions, and comparing a mix of high and low performers (in terms of self-reported partnership success).*
- Statistical correlation analyses using Spearman's rho were conducted on the data. The statistical analyses in this report do not confirm causal relationships between any specific variables and outcomes (though in some cases they are suggestive of a causal relationship, particularly when combined with qualitative data and analysis).
- Specific Spearman's rho values for the correlations shown may be found in the appendix. Below is a guide to understanding how they were interpreted in this study:

Spearman's rho value	Interpretation
0 – (±) 0.2	No correlation
(±) 0.2 — (±) 0.4	Low correlation
(±) 0.4 — (±) 0.6	Moderate correlation
(±) 0.6 — (±) 0.8	Significant correlation
(±) 0.8 — (±) 1.0	High correlation

Table 1

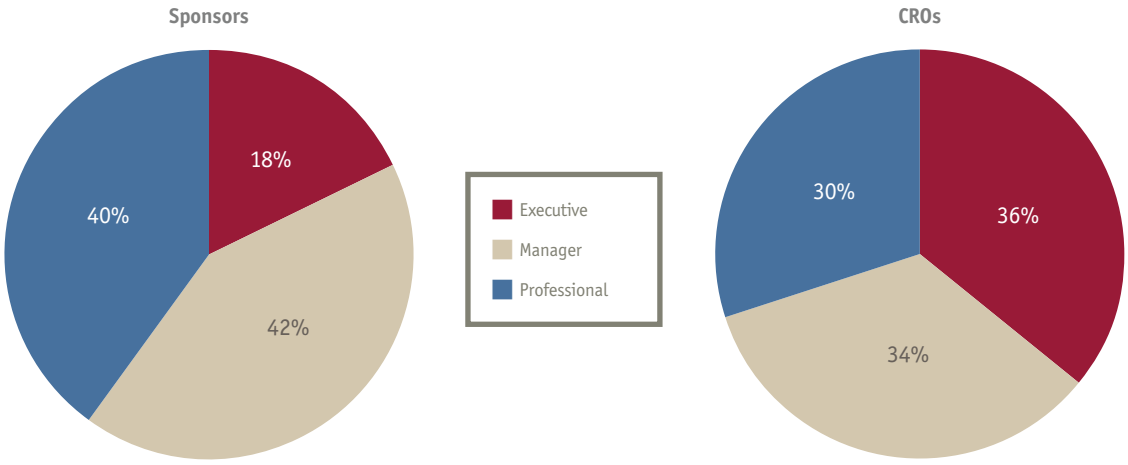
* Note: 10% of respondents did not disclose title.

Study participant demographic breakdown



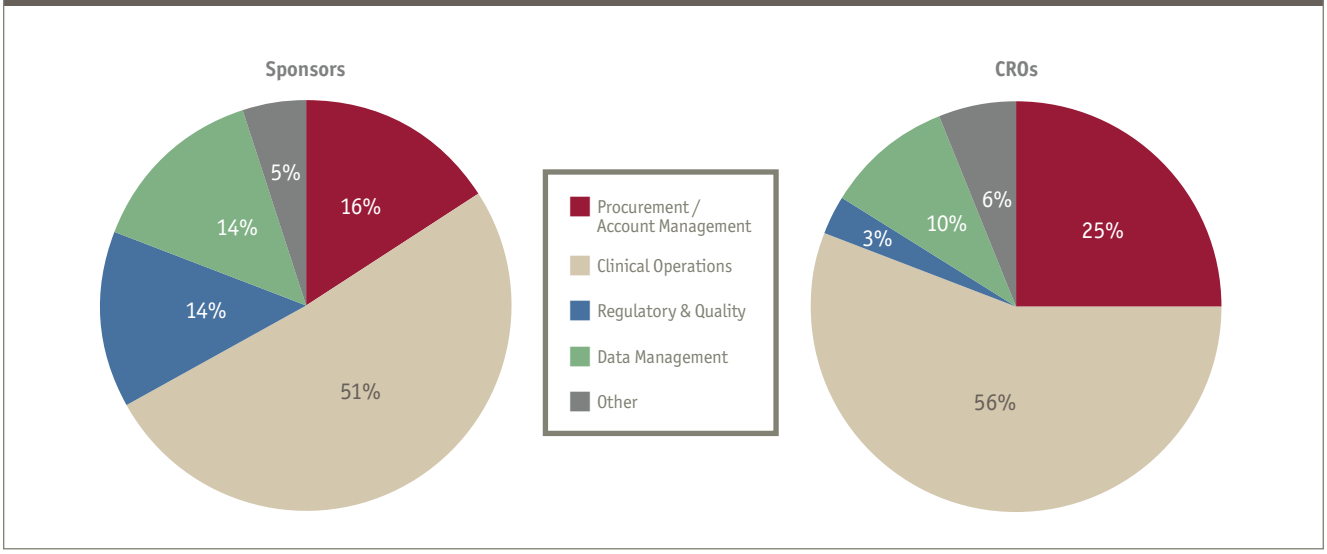
Graph 1

Study participant demographic breakdown — by role



Graph 2

Study participant demographic breakdown — by function



Graph 3

Part Two

Background and related research

The largest pharmaceutical companies outsource nearly 100% of laboratory services (central and bioanalytical), as well as Phase IIIB and Phase IV studies, to CROs.

The pharmaceutical industry faces enormous pressure to bring new, innovative medicines to market more quickly, at lower cost

- According to the United States Food and Drug Administration (USFDA), the annual volume of drug approvals has declined by 50% during the past decade (to just 15 per year). At the same time, spending on research and development has nearly doubled to $45B per year.[1]
- Revenue-at-risk in the pharmaceutical industry is expected to reach an unprecedented $125B in the next several years, due to patent expirations and the rise of generic competition.[2]
- In 2011 alone, ten medicines with combined annual sales of nearly $50B came off patent.[2]
- The average cost to bring a new drug to market (from discovery through trials and approval) is estimated to be approximately $1.2B, spread across a 15 year development cycle.[3,4] Out-of-pocket development costs associated with clinical trials are substantial — totaling approximately $216M per drug (see Table 2).

Mean out-of-pocket development costs for an individual drug[5]

Phase I	Phase II	Phase III	Total
$16M	$42M	$158M	$216M

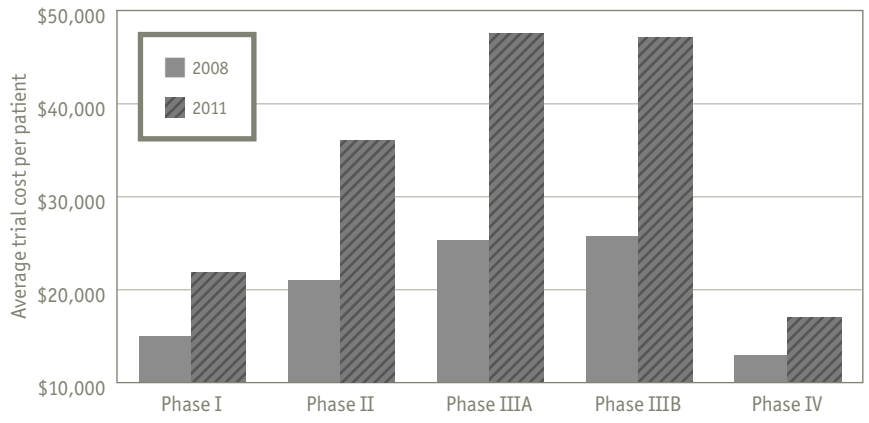
Table 2

- Unfortunately, only 21.5% of all drugs that begin Phase I trials eventually make it to the market. Meaning, if you assume spending is spread equally across all drugs, as much as $5.08B is spent each year on drugs that will never make it to the market.[6]
- Average per-patient trial costs, across all therapeutic areas and phases, increased 63% between 2008 and 2011 (see Graph 4).[7]

The use of clinical research organizations (CROs) as outsourcing providers for clinical development work has risen sharply

- The use of CROs across all therapeutic areas and phases has increased 44% in the past four years.[8] Today, the largest pharmaceutical companies outsource nearly 100% of laboratory services (central and bioanalytical), as well as Phase IIIB and Phase IV studies, to CROs.[9]
- CRO industry revenues have grown 156% since 2001.[7] In 2010, for the first time, CROs had more head count in support of pharmaceutical research and development than pharmaceutical and biopharmaceutical companies.[10]

Rising costs of clinical trials[7]

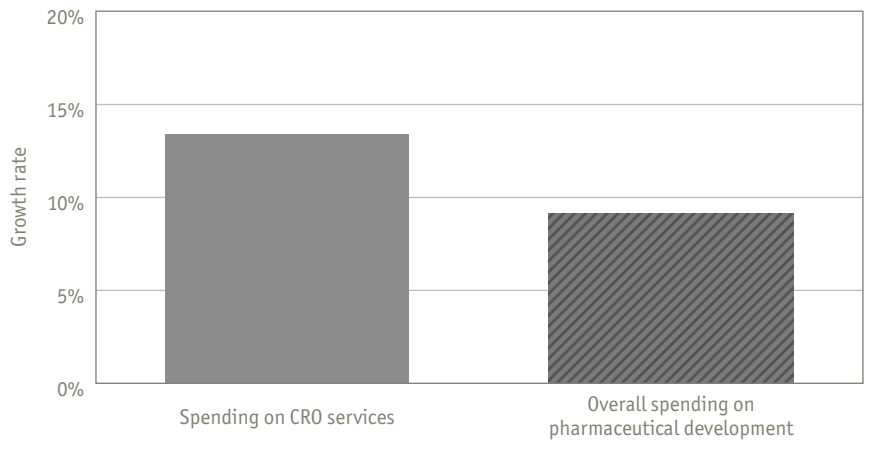


Graph 4

> "While pharmaceutical companies are increasingly outsourcing development work to CROs, perceptions regarding performance are mixed."
>
> — Director of Procurement Operations, Healthcare Sector

- CROs were involved in the development of 33 of the 38 new medicines approved for use in the United States and Europe during 2010.[7]
- During 2011, biotechnology and pharmaceutical companies spent more than $28B on contract clinical service providers (net of pass through costs such as central lab fees and investigator grants, which often amount to 30 – 40% of an overall trial budget).[11]
- Since 2001, annual growth in spending on CRO services has dramatically outpaced annual growth in overall spending on pharmaceutical development (13.4% compared to just 9.1%).[12]

Annual growth since 2001[11]



Graph 5

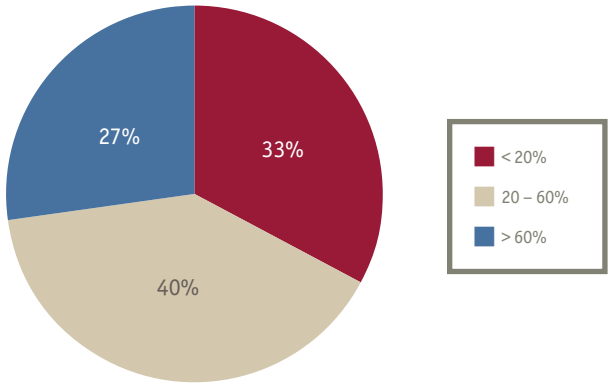
Partnering for expansion

In a 2011 press release, Takeda cited "facilitat[ing] Takeda's global growth" as a key reason for launching partnerships with CRO giants Covance and Quintiles. Clearly, they hope that closer collaboration will allow them to more effectively leverage the capabilities and resources of these CROs to drive growth in emerging markets, such as those in Asia.

Sponsors believe that, in general, outsourcing clinical trials is preferable to relying on internal resources

- Sponsors frequently cite the following pressures as reasons for shifting clinical trial work to CROs: enabling increased focus on core competencies, a need to augment staff due to downsizing, increased trial volume, a need to control costs, and increased safety requirements.[13]
- Some evidence suggests that clinical trials conducted using CROs are, on average, completed 30% faster than in-house trials — without sacrificing data quality.[14]
- During a presentation at the Partnerships in Clinical Trials Conference in early 2011, financial analyst Steve Unger of Lazard Capital Markets asserted that trials conducted by CROs have proven to be "better, faster, and cheaper" than those done in-house.
- Sponsors report that outsourcing clinical trials provides opportunities to expand their global reach; to leverage knowledge that CROs have about operating in other geographic markets; and to leverage CRO expertise in specific functional areas, such as patient recruitment or data management.

Percentage of drug development budgets spent on outsourcing



Graph 6

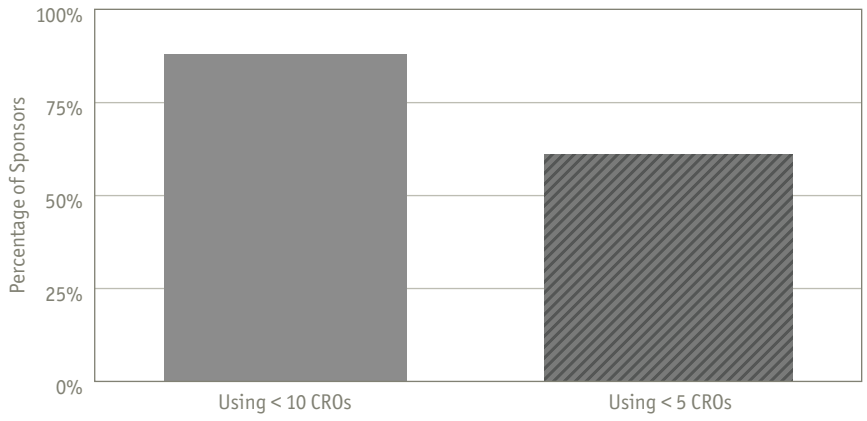
The Life Sciences industry has, and will likely continue to, move away from transactional relationships between CROs and Sponsors — and toward closer, more collaborative partnerships between Sponsors and CROs

- For many years, Sponsors worked with CROs primarily through transactional, ad hoc contracts that amounted to what Andrew Bonfield, former chief financial officer of Bristol-Myers Squibb has referred to as "out-tasking".[15] These arrangements enabled pharmaceutical companies to access flexible capacity for clinical development work, but were inadequate to deliver any of the other benefits commonly found in true outsourcing arrangements (e.g., increased efficiency and innovation).
- Approximately ten years ago, Sponsors began to form closer relationships through preferred supplier agreements. However, even under these agreements, Sponsors typically continued to bid out individual trials separately, CROs were not guaranteed any specific amount of work, and Sponsors did not shed assets or significantly reduce their internal cost structures. Sponsors and CROs often gained some benefit in the form of more efficient commercial transactions, but did little to enhance operational integration or expand collaboration on study design and planning.
- Over the past several years, an increasing number of companies have entered into more strategic partnerships with a small number of CROs and/or other providers of specific services such as data management or central labs. In some cases, such arrangements are partnerships in name only, and mainly entail consolidation of outsourced services with a smaller number of suppliers. In other cases, Sponsors and CROs (and/or other service providers) have implemented formal governance structures to improve strategic and operational integration, and enable more efficient and effective issue resolution; have invested in joint training and common systems on the back of long-term commitments to continue working together; and, more recently, have begun to move away from pay-for-activity and toward pay-for-performance arrangements. These more mature manifestations of partnership have been effective in other industries and outsourcing contexts, and we believe they can deliver significant benefits to all parties involved in the drug development process (see Graph 7).[12]
- Many smaller biotechnology firms have been working with CROs in collaborative partnerships for a long time. Increasingly, large pharmaceutical companies are adopting the same model — though the inertia associated with a long history of internal clinical development, and substantial extant internal clinical development resources, make this transition slower and more difficult.

> "Our pipeline is small now compared to what it was five years ago. We used to run 150 studies and we had a lot of vendors. I could have someone running five studies with five vendors... Now that we have fewer studies and fewer internal resources, it is much easier for my team to work with two vendors than five, 25, or 50 vendors."
>
> — Director, Data Management, Global Pharmaceutical Company

These more mature manifestations of partnership have been effective in other industries and outsourcing contexts, and we believe they can deliver significant benefits to all parties involved in the drug development process.

Shift toward using fewer CROs



Graph 7

Portion of CRO Revenue by Type of Relationship with Sponsor[16]

Type of relationship	Large CROs	Niche / mid-size CROs
Transactional services	29%	59%
Functional service provider	22%	19%
Integrated alliance services	39%	22%

Table 3

Respondent characterizations of current Sponsor-CRO relationships

Graph 8

Part Three

Outcomes (to-date) of the shift toward partnerships between Sponsors and CROs

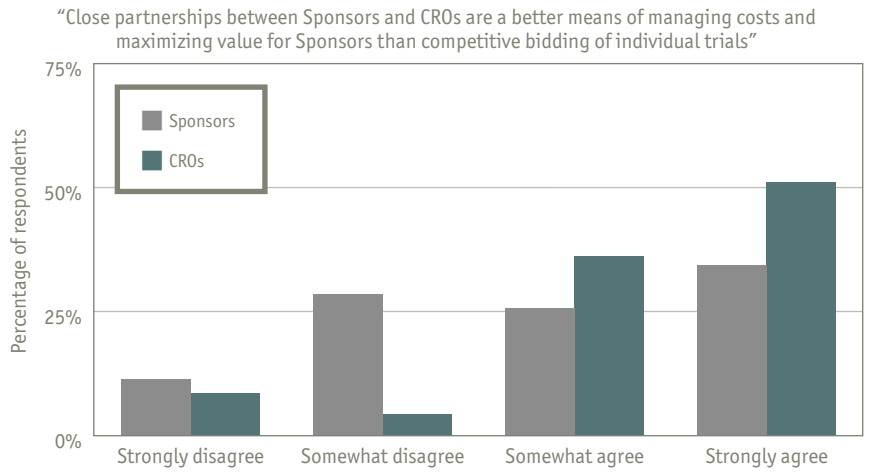
> "When you have multiple vendors, every vendor has differences that make problems when you try to bring it together and submit to the USFDA. We've eliminated some of that by selecting a strategic partner to work with."
>
> — Program Manager, Global Pharmaceutical Company

Both Sponsors and CROs expect strategic partnerships to deliver considerably more value than traditional arrangements

Vantage conducted a global, cross-industry study of collaboration between customers and their key suppliers, the findings of which reinforce the perception that close partnerships between CROs and Sponsors are a better means of managing costs and increasing value for Sponsors than a transactional model that involves competitive bidding of individual trials.[17]

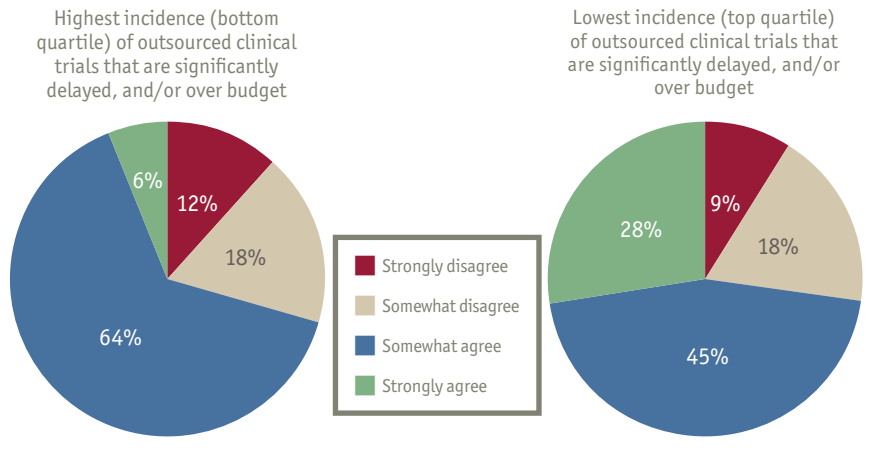
- Customers reported realizing, on average, 40% more value from their most collaborative key suppliers compared to their least collaborative key suppliers. Life Sciences companies in particular reported realizing, on average, 49% more value.
- Suppliers reported delivering, on average, 49% more value to their most collaborative key customers compared to their least collaborative key customers. Suppliers to the Life Sciences sector in particular reported delivering, on average, 23% more value to their most collaborative key customers.
- Our broad findings accord with numerous case studies demonstrating that collaborative relationships between customers and suppliers, characterized by high levels of trust and mutual respect, robust communication, and increased strategic and operational integration, deliver substantial benefits to companies that are able to systematically build and sustain them. Lower transaction costs, increased transparency, and an increased willingness to invest in a relationship, by both parties, reliably lowers costs and reduces risks for both sides, and facilitates significantly higher levels of innovation.
- Closer, more collaborative relationships have the potential to save both Sponsors and CROs time and money, as well as deliver other benefits such as increased patient safety, improved regulatory compliance, and enhanced quality of trial data. The means by which such benefits are achieved include:
  - Enabling early engagement between Sponsor and CRO in protocol design and study planning — which is very difficult, if not impossible, under a transactional model where competitive bidding precedes any engagement with a CRO or service provider
  - Reducing transaction costs associated with the need for RFP development, bid submission, and evaluation at the start of every clinical study
  - Increasing willingness to invest in joint training, improved systems, after-action analysis of clinical studies, and in general, to work together to jointly drive continuous improvement of the clinical development process
  - Enabling both Sponsors and CROs to build up tacit knowledge about how to work together effectively

Relative strength of close partnerships versus competitive bidding regarding managing costs and maximizing value for Sponsors



Graph 9

More seamless collaboration between Sponsors and CROs is correlated with Sponsors reporting trials completed on time, and at or under budget



Graph 10

Closer, more collaborative relationships have the potential to save both Sponsors and CROs time and money, as well as deliver other benefits such as increased patient safety, improved regulatory compliance, and enhanced quality of trial data.

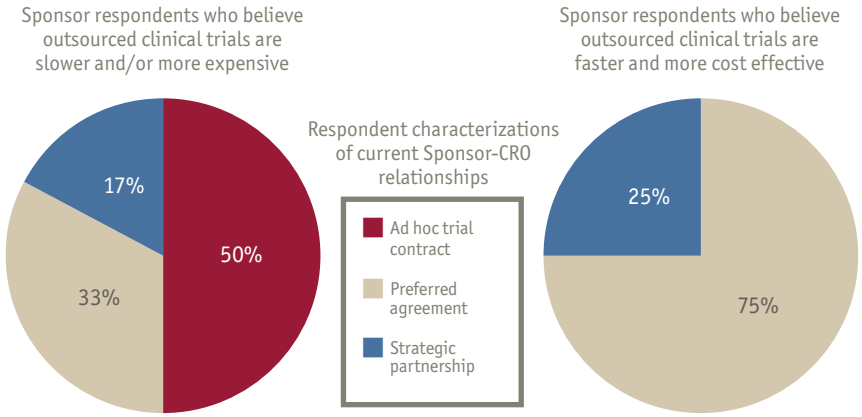
> "We want to be having different types of conversations with our strategic partners early. We've done analysis on the bid process. Developing a proposal can cost up to $50k and when we go to bid defense, that's another $50k easy. That's $100k we could be investing in conversations that actually make the program better, rather than throwing it away on fighting over business."
>
> — Account Manager, Global CRO

The USFDA estimates that only 6% of clinical trials are completed on time.

"I don't have data, but I really don't think we get anything faster or cheaper with CROs. They resource the projects based on their internal prioritization. If we aren't their biggest customer, we don't get the resources and they don't fix problems quickly enough. Then, we don't hit our goals."

— SVP, Clinical Science, Mid-Sized Pharmaceutical Company

A strategic partnership with CROs is correlated with Sponsors reporting that outsourced trials are faster and more cost effective

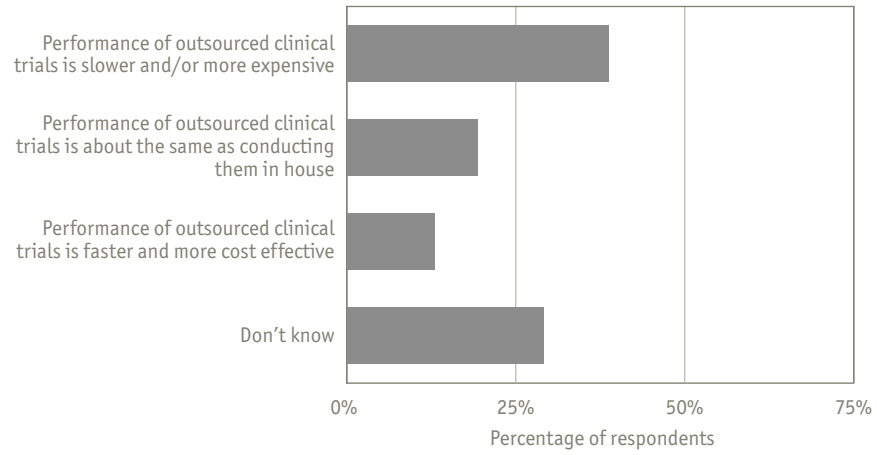


Graph 11

Despite the promise of collaborative partnerships between Sponsors and CROs, many partnerships fail to deliver value commensurate with expectations

- Despite the dramatic shift in recent years toward using CROs more heavily, and the perception that such partnerships should yield benefits, Sponsors still report mixed results. The USFDA estimates that only 6% of clinical trials are completed on time, and 72% of trials run over schedule by more than one month.[18] Only a minority of Sponsors in our study report finding outsourcing to CROs faster and more efficient; a large number of Sponsors (29%) are not sure.
- Though there is evidence that CROs can reduce costs, speed time to market, and even enhance quality, case study analysis (along with our own experience working with clients) suggests that most outsourced clinical trials continue to suffer from significant cost, quality, and efficiency challenges. The data in Graph 11 indicate the extent to which Sponsors lack the requisite information and/or tools to effectively compare the true total costs of clinical trials conducted in-house versus those that are outsourced. The lack of objective, usefully analyzed data allows various biases to warp perceptions of the relative costs and benefits of outsourced clinical development.
- Of the ten major Life Sciences companies that we interviewed, only two felt they were able to rigorously measure and compare the true cost of internal versus outsourced clinical trials. Better tools and processes for measuring the

Performance of outsourced clinical trials versus the performance of trials conducted in-house — per Sponsors



Graph 12

cost, performance, and value of internal versus outsourced clinical activities are essential if bio-pharmaceutical companies are to make optimal choices about what to outsource and what to do with internal resources.

There are a number of factors that contribute to the under-performance of many Sponsor-CRO partnerships

- Sponsors report that 70% of trials conducted with CROs end up requiring more time and/or resources than originally anticipated. This perception exists even at Sponsors that are engaged in strategic partnerships with CROs.
- The frustration is not limited to the Sponsor side. CROs report performing significant amounts of out-of-scope work for little or no additional compensation. While CROs attempt to recoup costs associated with changes to requirements or project scope, they are not always successful. Many CROs perceive that the root cause behind over-budget and over-time trials is not the ability of CROs to effectively execute the trial, but rather, the additional work required by scope and protocol changes (many of them avoidable). The Tufts Center for the Study of Drug Development estimates that:
  - More than half of all protocols require at least one amendment (with later stage trials having the highest average number of amendments)
  - One-third of all amendments are avoidable
  - Each amendment adds approximately two months and $500k to a clinical trial[19]

Sponsors report that 70% of trials conducted with CROs end up requiring more time and/or resources than originally anticipated.

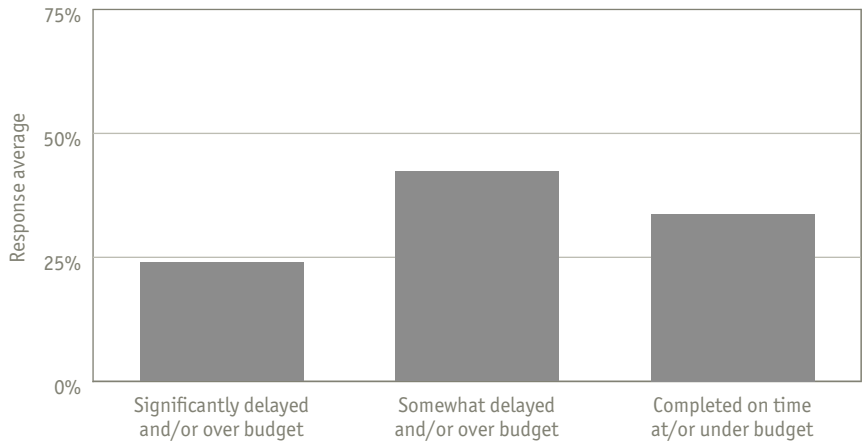
"[In the past], clients didn't have cost controls and an approximation was enough. Now, they want a firm quote. They want us to be completely responsible for third party vendors, take on all the risk. The problem is, we don't get firm quotes from our vendors and we struggle to assess these costs accurately."

— Director of Contracting (Europe), Global CRO

Management of third-party expenses

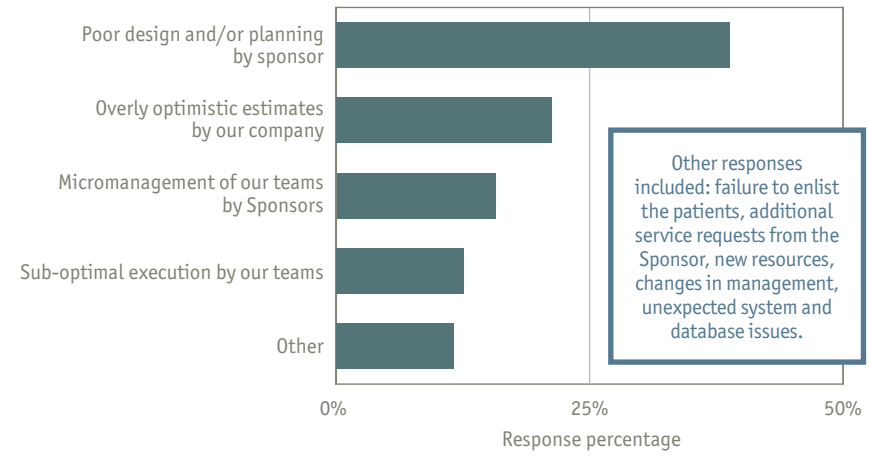
Sponsors are increasingly asking CROs to assume a larger share of the risk associated with conducting clinical trials. In more transactional relationships, contracts are typically time-and-materials based, where Sponsors retain control over third-party vendors (e.g., couriers) regardless of whether vendors work directly with CROs. In many strategic partnerships, some of these costs are increasingly absorbed by CROs, rather than passed through to Sponsors. For CROs, this can result in expanded control over study components, opportunities to increase efficiencies with strategic suppliers, and increased profitability; however it also increases the risk borne by CROs, particularly when costs exceed projections due to circumstances beyond the control of CROs. Costs for CROs are now increasingly front-loaded, and analysts are, at present, unable to quantify the value of these arrangements.

Performance against scope of clinical trials — per Sponsors



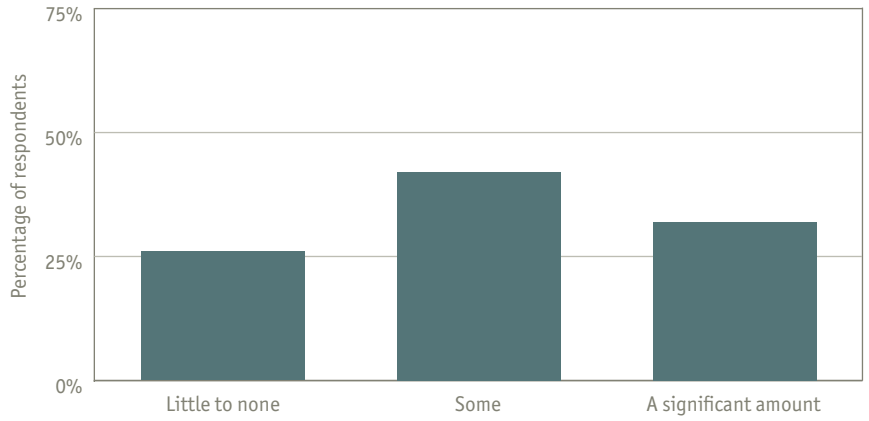
Graph 13

Reported causes for delayed or over budgeted clinical trials — per CROs



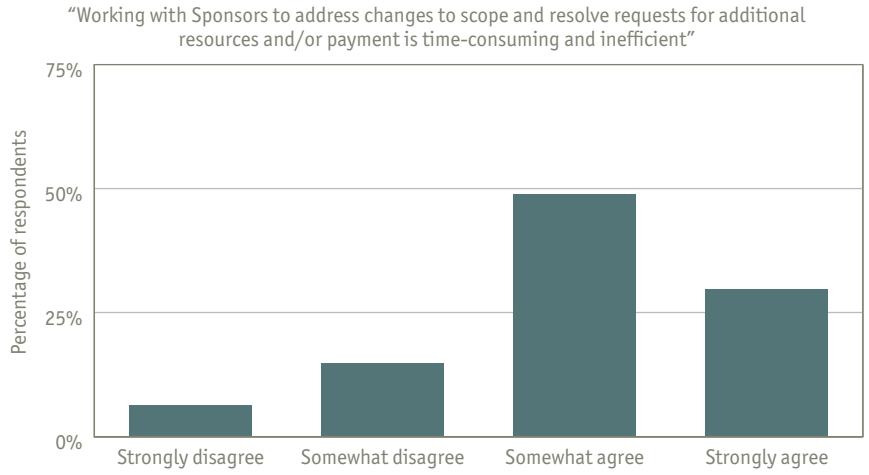
Graph 14

Amount of "out-of-scope" work performed for Sponsors on clinical trials, without additional compensation — per CROs



Graph 15

Cost of resolving requests for additional resources and/or payment — per CROs



Graph 16

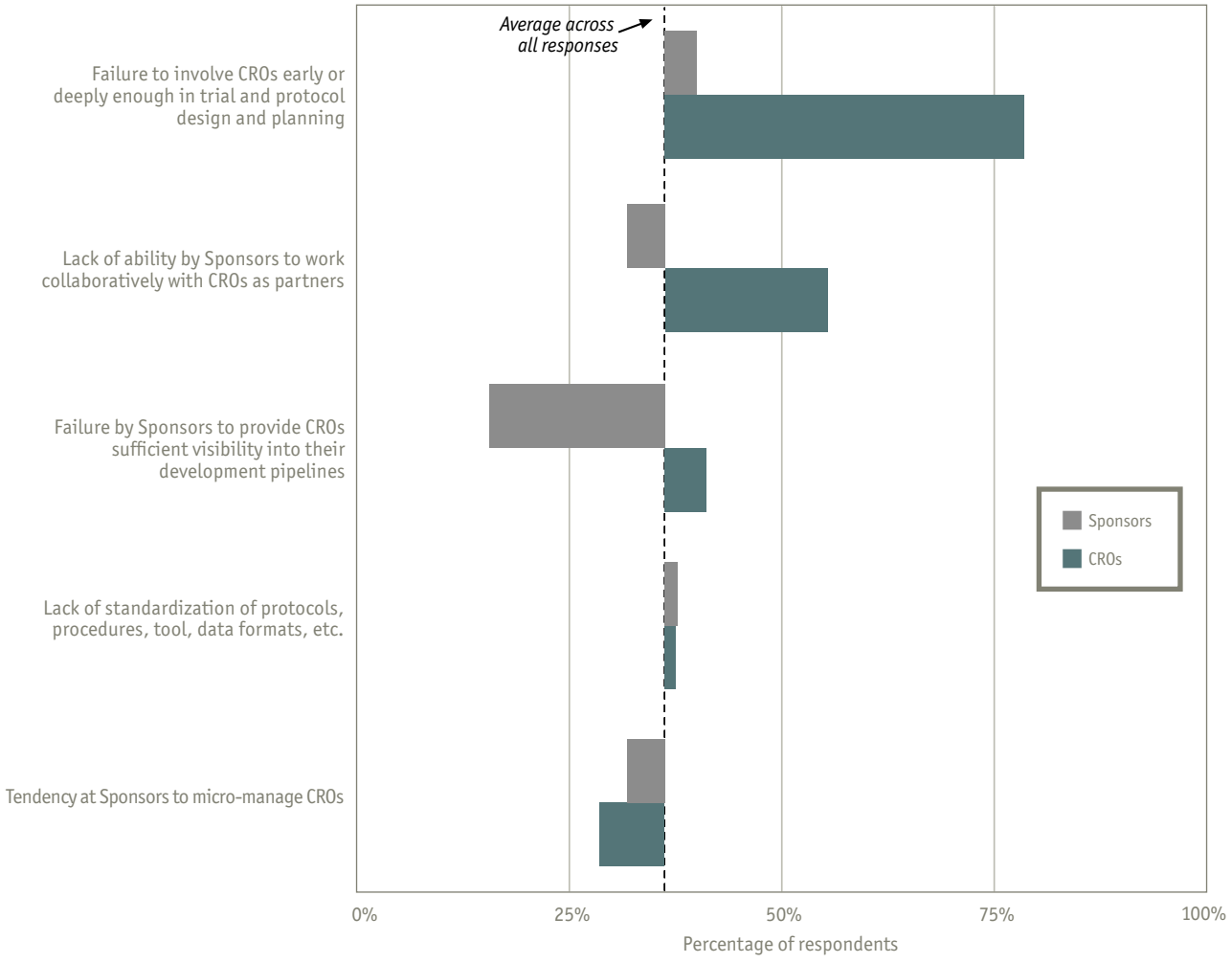
> "Every one of our trials has gone over budget; I don't know the average amount. I can't think of a project where we haven't done 20 change orders. This is a problem both sides have created."
>
> — Head of Outsourcing, Global Pharmaceutical Company

In the remainder of this report, we investigate the challenges Sponsors and CROs face as they seek to move toward a more strategic and less transactional way of working together. We then provide concrete advice on best practices to enable both Sponsors and CROs to systematically improve the speed, quality, and costs associated with outsourced clinical development.

Part Four

Barriers to reducing costs and improving quality and efficiency

Top reported barriers to maximizing the efficiency and total value delivered through the outsourcing of clinical trials

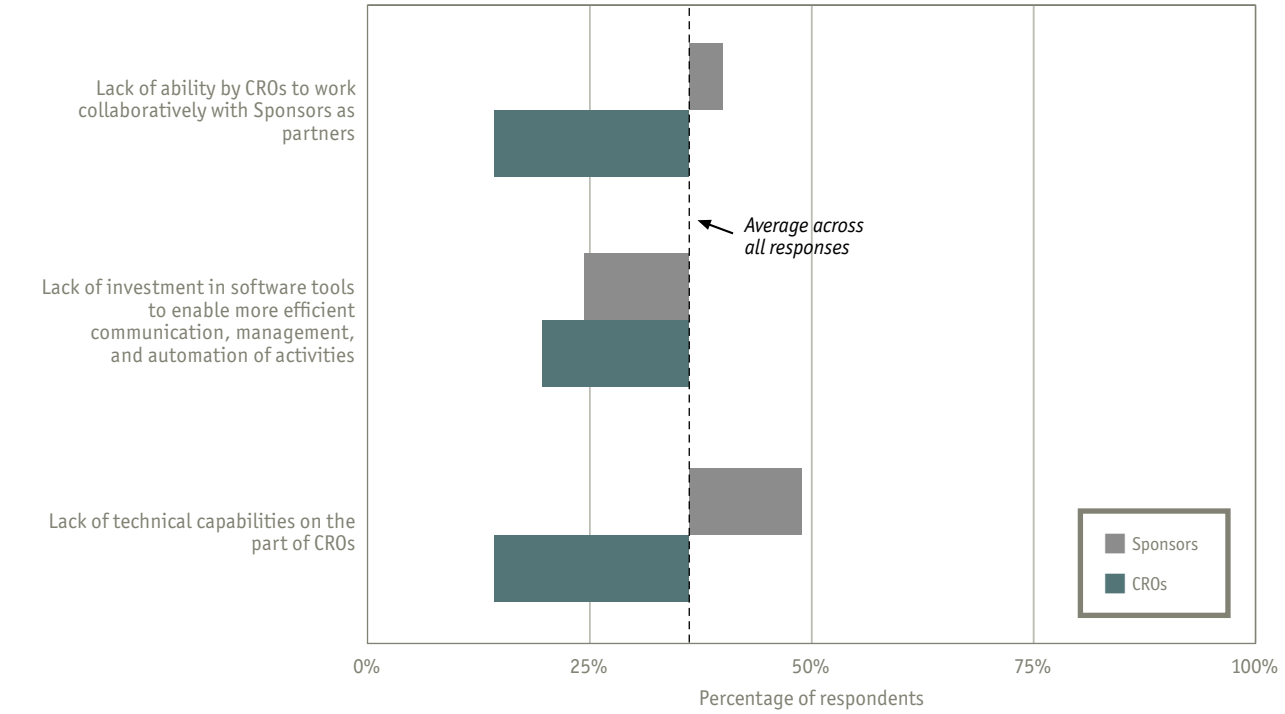


The "average across all responses" line is an average (across all noted barriers) of the percentage of study respondents who noted a barrier as "significant" (across both CROs and Sponsors).

The further a bar extends to the right of this line, the more respondents noted the specific barrier as significant relative to all the barriers surveyed. Conversely, the further a bar extends to the left of the dotted average-response line, the fewer respondents noted the specific barrier as significant.

Graph 17

Other reported barriers to maximizing the efficiency and total value delivered through the outsourcing of clinical trials



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The further a bar extends to the right of this line, the more respondents noted the specific barrier as significant relative to all the barriers surveyed. Conversely, the further a bar extends to the left of the dotted average-response line, the fewer respondents noted the specific barrier as significant.

Graph 18

As the graphs show, there are a number of barriers that impede the ability of Sponsors and CROs to collaborate in an optimal fashion, and hamper efforts to reduce the time and cost associated with conducting clinical trials. Not surprisingly, Sponsors and CROs often differ in their perceptions of the root causes of difficulties — and because these different perceptions are often not rigorously and jointly explored, they act as a further barrier to improvement. Unless Sponsors and CROs sit down as partners and jointly discuss barriers to improvement, it is unlikely that significant progress will be made.

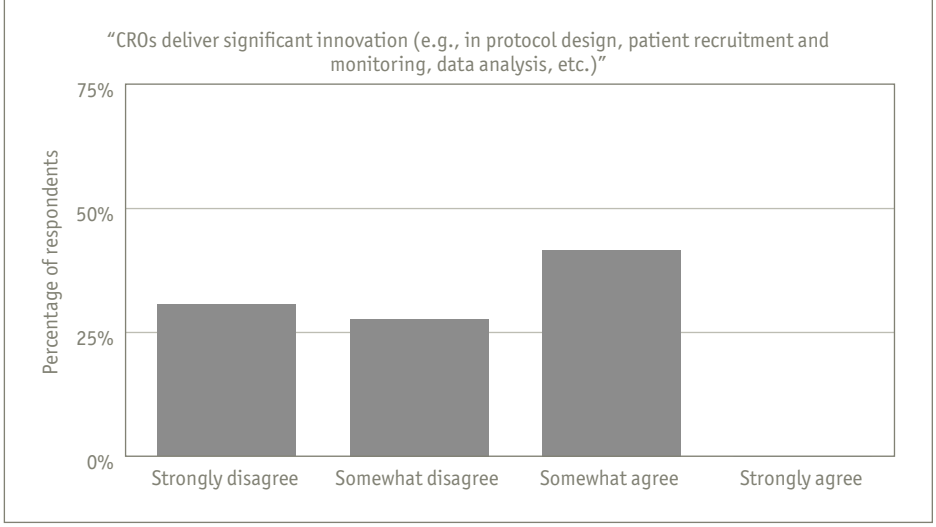
Failure to involve CROs early or deeply enough in trial and protocol design and planning

> "There is one Sponsor with whom we have regular conversations about trials while they are still in the planning stages. We've been able to say, 'There is extra capacity in X or Y country, we can give you a discount if you run that trial there.' It has been a big help to both of us."
>
> — Clinical Operations, Global CRO

- CROs consistently report frustration that Sponsors either do not provide opportunities for them to give input into protocol design and study planning, or do not listen to or act on their input when it is given. Yet there are a number of key considerations in planning a clinical trial for which CROs often hold useful information:
  1. Where are the sites with the highest recruitment potential and which investigators have the best track record (in terms of both recruitment and protocol execution)?
  2. What challenges have other companies run into when executing studies of this type and/or in these regions?
  3. What are the adverse events that could derail the timeline? How likely are they? What has been done in other trials to mitigate or eliminate these risks (by Sponsors, by CROs, and/or together)?
- Conversely, numerous Sponsors lament that their CROs (even within the context of a strategic partnership) fail to bring forward suggestions on how to do things more quickly and/or efficiently. In fact, not a single Sponsor in our study reported that their CROs deliver significant innovation.
- Historically, Sponsors have put significant time and effort into developing the protocol, plan, and timeline, for a study long before they engage with CROs. Even when the process for engaging with CROs specifically includes opportunities

> "We have a place in our RFPs where we ask our CRO partners to provide us with suggestions that would reduce timelines or cost and/or improve quality. However, I don't think we've ever changed our plans as a result of their input. I'm frankly not sure if we even *consider* changing our plans."
>
> — Outsourcing Manager, US-based Pharmaceutical Company

The degree to which CROs deliver significant innovation — per Sponsors



Graph 19

for CROs to provide input, they often come far too late, when time pressures, inertia, and personal investment in the design (on the part of individuals at Sponsors) create substantial barriers to adopting any new ideas from CROs.

- Reducing reliance on competitive bidding addresses one major barrier to early collaboration. Even so, many companies that have made the shift toward strategic partnerships have not changed their systems, processes, and behaviors related to clinical research program design, planning, and execution. The existing infrastructure and sourcing culture all support limited interaction and collaboration prior to the decision to begin work with CROs on a study.
- Providing meaningful input into the design of a protocol requires CROs to invest time and resources in both developing ideas and vetting them with Sponsors. Who ought to pay for this work — should CROs absorb costs, or should Sponsors reimburse them? The challenge of determining how much up front engagement should occur and who should pay for it becomes even greater when there is more than one supplier who may be awarded all or part of the work.

Failure by Sponsors to provide CROs sufficient visibility into their development pipelines

- CROs report that having little (or no) visibility into the pipelines of their Sponsors makes it difficult for them to forecast demand, and therefore creates numerous costs and delays at the start of new trials. Sponsors, however — by a very large margin — list limited CRO visibility into development pipelines as the least significant barrier to increased outsourcing effectiveness. Consistent with this perception, few Sponsors report providing such visibility to their CRO partners.
- In our experience, this phenomenon has two causes:
  1. Sponsors (especially those with more than one CRO partner) worry that discussions about programs and trials that *might* start soon and *might* involve CROs would either have no impact on CROs' investment plans, or lead to inappropriate investments by CROs, as they plan for work that is still subject to potential delay or cancellation.
  2. Sponsors also worry that through inattentiveness, lack of controls, and/or other means, individuals at CROs might leak confidential information to the marketplace.

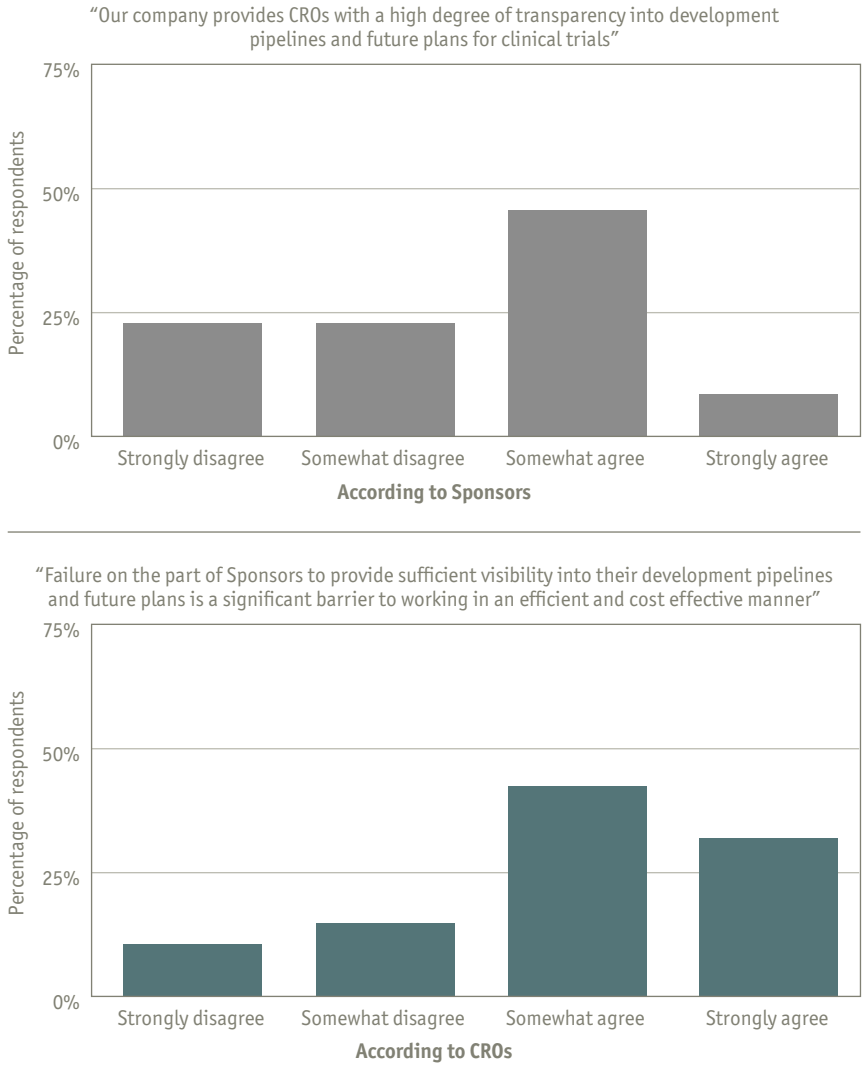
Few Sponsors report delivering much in the way of visibility to their CRO partners.

> "We need to determine a way to build enough trust to involve our CRO in study design. [Study design] is where your biggest detractors will not want people from a CRO getting involved and saying: 'If you do this we can do that faster or these countries should be considered.' Our CRO is normally engaged very late in the game. Getting them involved earlier and brainstorming and designing things together will be a big culture shift."
>
> — Head of Development, Global Pharmaceutical Company

"We often use the same name for a report, and therefore think we're all aligned. Then, we get down to the end and find out that what we (the Sponsor) meant was *very* different from what our CRO meant. Of course, we end up having to pay a change fee because we want more than they scoped into the contract."

— Study Manager,
US Pharmaceutical Company

Transparency into development pipelines and future plans

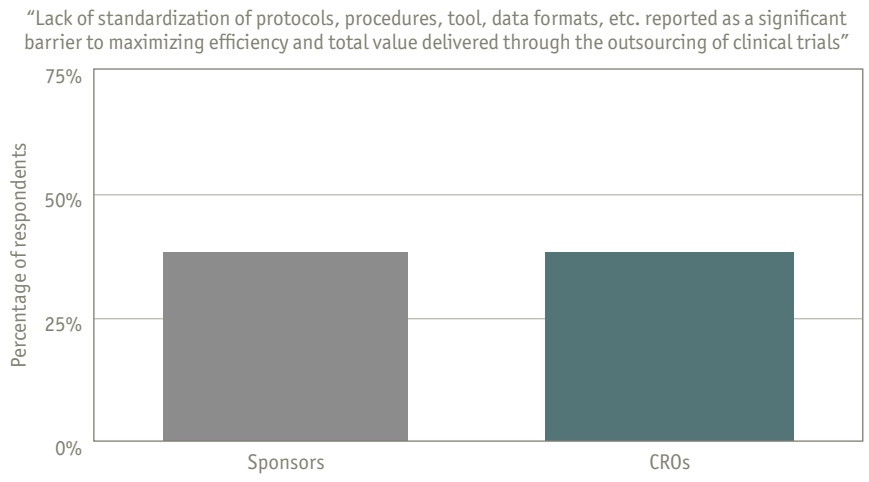


Graph 20

Lack of standardization (of protocols, procedures, tools, data formats, etc.) and lack of investment in software tools to enable communication, management, and automation of activities

- There is a significant, though not surprising, lack of standardization in the clinical trial industry — both across and within Sponsors and CROs.
  - In one study, 97% of respondents (in clinical development roles across the pharmaceutical and clinical research industries) reported that it would be valuable if the content and format of data collection instruments were standardized.[20]
  - In another study, 50% of participants reported that physician (and, by extension, patient) recruitment could be improved through the creation and use of a more comprehensive online marketplace or clearinghouse.[21] Currently, several CROs and several Sponsors have developed and manage their own databases of investigators; none of these are comprehensive.
- Many larger pharmaceutical companies are the result of numerous mergers, some of which have never been fully integrated, and which consequently retain their own legacy processes and methodologies. In addition, these companies span across multiple regions that often require different approaches and outcomes (due to differences in the marketplace and/or regulatory environment).
- CROs have historically been required to follow each Sponsor's internal approaches — meaning each CRO has almost as many ways of conducting a trial as it has Sponsors. In a report by PPD (one of the top 10 CROs globally),

Degree to which Sponsors and CROs report lack of standardized procedures as a barrier to realizing more value



Graph 21

Each CRO has almost as many ways of conducting a trial as it has Sponsors.

> "[The Sponsor] always has specific things they are looking for that they never describe to us. When we realize they want something "out-of-scope" and point it out, they are shocked. They seem to think, 'How else could you possibly meet the milestone?'"
>
> — Director, Clinical Project Management, Global CRO

> "We are constantly complaining about our CRO, but not looking to ourselves to see if we're sending inconsistent messages. If one clinical team says, 'Do it this way' and another clinical team says, 'Do it that way,' how can our CRO have a consistent process?"
>
> — VP, Clinical Development (EU), Mid-Sized Pharmaceutical Company

Dr. Harris Dalrymple noted, "Some clients have a rigorous set of systems and demand all studies adhere to all client systems. [And], some clients are internally inconsistent and use different systems for the same activity."[22]

- As Sponsors and CROs have begun to work with each other in more long-term, collaborative relationships, many have recognized that failing to define common standards leads to significant inefficiencies, and hinders their ability to realize cost savings — as well as compromising quality and safety. But they have also found that tackling standardization is not easy.
  - Individuals within Sponsors are generally very attached to their own way of doing things and resistant to change — especially when some trials, or some of the work on trials, will still be done internally.
  - The sheer number and complexity of things that would benefit from review and standardization (processes, tools, data systems, etc.) is so great, and timelines for conducting trials are so short that both Sponsors and CROs often decide to "focus on the trials" and leave standardization work for the future when there is more time — which of course, never happens.

New tools have improved communication between CROs and Sponsors and enabled greater standardization of processes and reports within and across trials

- Using technology-enabled systems and processes (software tools) to deploy resources more efficiently in a Phase II trial yielded a 30% cost reduction (more than $1M), according to Sponsor estimates.[24]
- Employing partnership portals has yielded less quantifiable, but anecdotally compelling, benefits for many Sponsors and CROs. Portals enable faster communication and lead to more effective knowledge management — especially when working on global teams.

Benefits to Sponsors of managing clinical trial documents with online tools (according to Sponsors)[23]

Saves time	41%
Helps me better organize study-related information	22%
Saves money	16%

- Some evidence suggests that using electronic data capture (EDC) may decrease trial costs by up to 25%. The percentage of new clinical trials using electronic data capture (EDC) has increased from 13% in 2003 to 64% in 2010.[25]

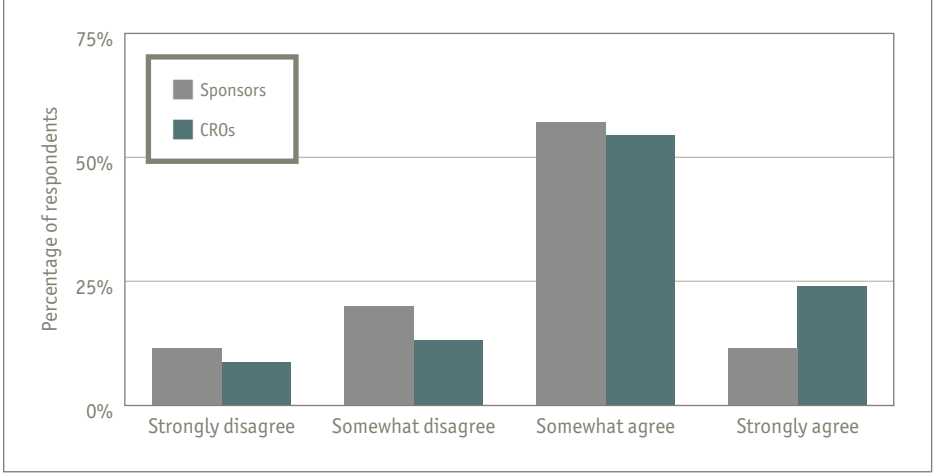
Table 4

Lack of ability by Sponsors and CROs to work collaboratively as partners

- One noteworthy (though not surprising) pattern in the data and our interviews is that Sponsors generally see a lack of collaborative behavior on the part of CROs as more frequent and/or more problematic than at their own companies. Likewise, CROs perceive more problematic behavior on the part of their Sponsors than their Sponsors perceive in themselves. While the survey participants were not necessarily customers and suppliers to one another, the general pattern is almost certainly reflective of natural human bias: we see the behavior of others as more suspect, and more problematic, than our own and we tend to see our own behavior as generally constructive and, at the very least, well intentioned.
- The assumptions and behaviors of both Sponsors and CROs often create a feedback loop within which both sides feel trapped and which neither side feels able to break.
- Developing a highly collaborative relationship (as described in Part Three) requires Sponsors and CROs to jointly reflect on the assumptions they bring to their interactions and plan together how to implement new ways of working with one another.

> "There is still the mentality that we are the Sponsor and they are the vendor, and we tell them what to do. Until we sit down as a team and make decisions together, that mentality won't change."
>
> — Head of Outsourcing Management, Mid-sized Pharmaceutical Company

Extent to which Sponsor-CRO staff collaborate seamlessly — as if they were members of the same organization

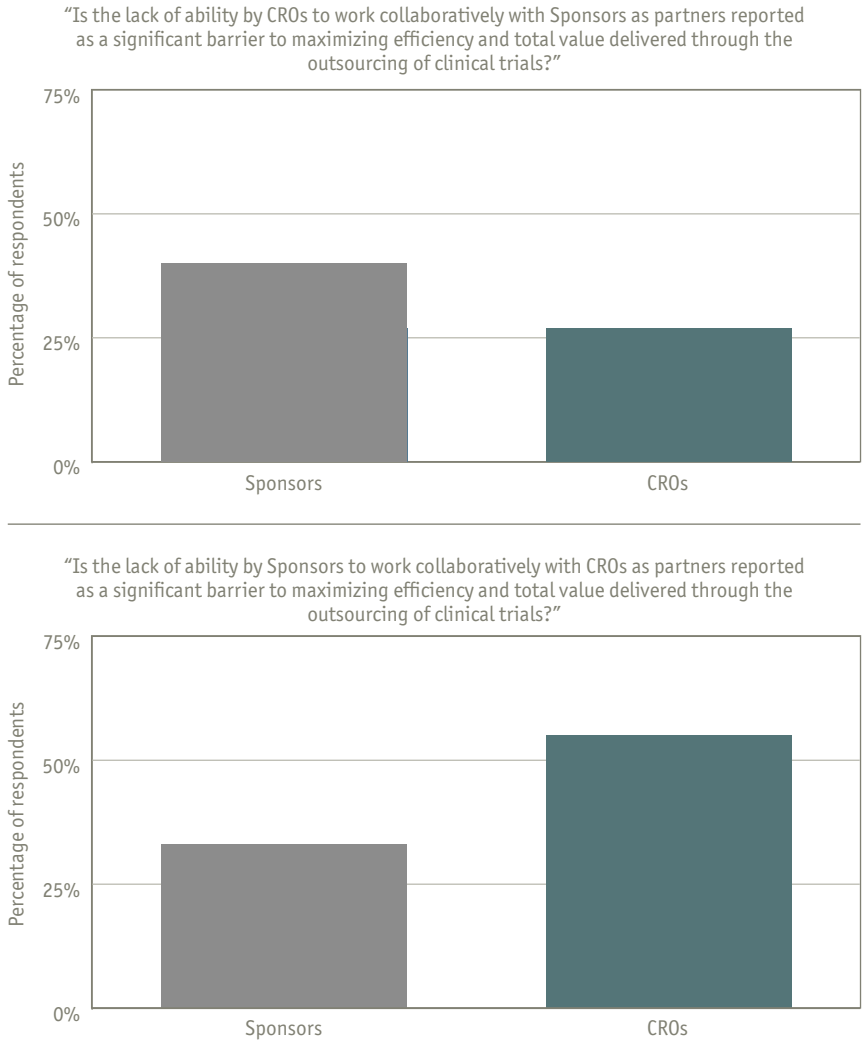


Graph 22

"I'm a little nervous because our Sponsor [in this new partnership] isn't articulating well what they want. We are trying to meet their needs, and I'm confident that we can. But, I'm a little worried about making sure we deliver to expectations, since I don't really know what the expectations are."

— Strategic Account Manager, Global CRO

Degree to which Sponsors and CROs report the lack of ability to work collaboratively as partners as a barrier to realizing more value



Graph 23

Common assumptions at Sponsors that lead to "un-collaborative" actions and sub-optimal results

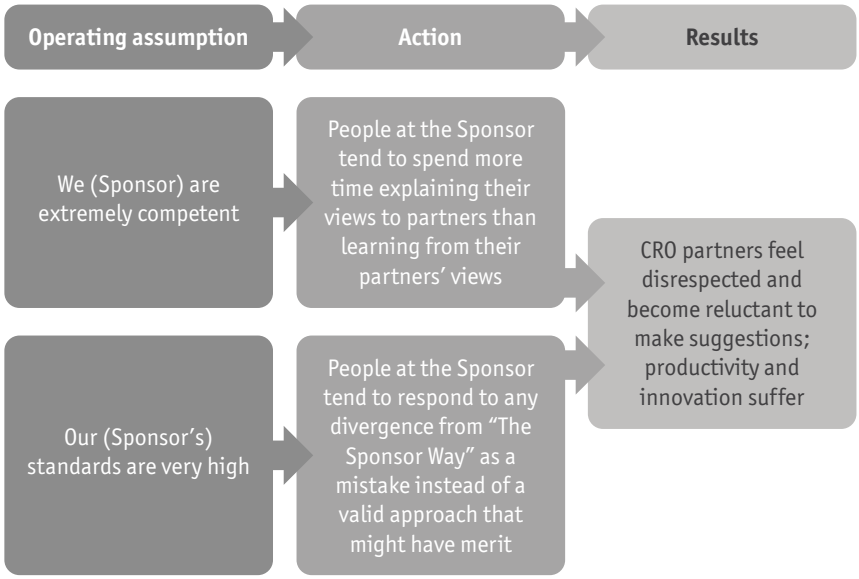


Figure 1

Common assumptions at CROs that lead to "un-collaborative" actions and sub-optimal results

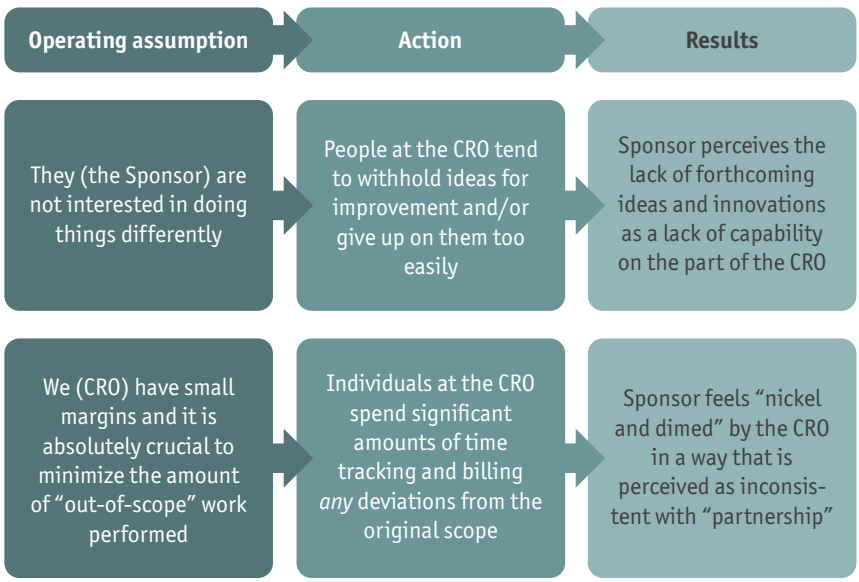


Figure 2

> "If we say 'do it our way' - that creates cost and challenges. If we say 'do it however' then it comes back in some weird format and we have to re-do it to get it in our format because it's unlikely to be what we want or expect. I'm not sure how to find the middle, so I just tell them 'do it our way.'"
>
> — Clinical Operations Specialist, Global Pharmaceutical Company

Case study: SOP overhaul

As one global pharmaceutical company experienced, overhauling SOPs requires a willingness to fundamentally shift perspectives. Disappointed with the amount of time and energy their teams were spending overseeing work by CRO partners, the company chartered a small team to develop a more effective oversight model. The team cataloged the activities that were still being done by Sponsor personnel and decided to look at each one in detail, to determine what could be shifted to CROs, and then prescribe what form of oversight would be most efficient and effective

They started with one they thought would be relatively straightforward — reviewing clinical research associate (CRA) trip reports. In the past, Sponsor personnel reviewed 100% of trip reports. Now, CROs were doing that. So, what did Sponsor personnel need to do to ensure CROs were doing a good job? The team started by suggesting that Sponsor personnel review 20% of all trip reports — a number that felt sufficiently large to say the Sponsor was providing oversight, while dramatically reducing the burden of review. Not surprisingly, however, there was substantial pushback from multiple groups. Regulatory worried that 20% might not be sufficient to meet the Sponsor's obligations. Quality questioned whether a sample of 20% would really ensure the trip reports were accurate and that all problems had been identified — How would the 20% be selected? (*cont.*)

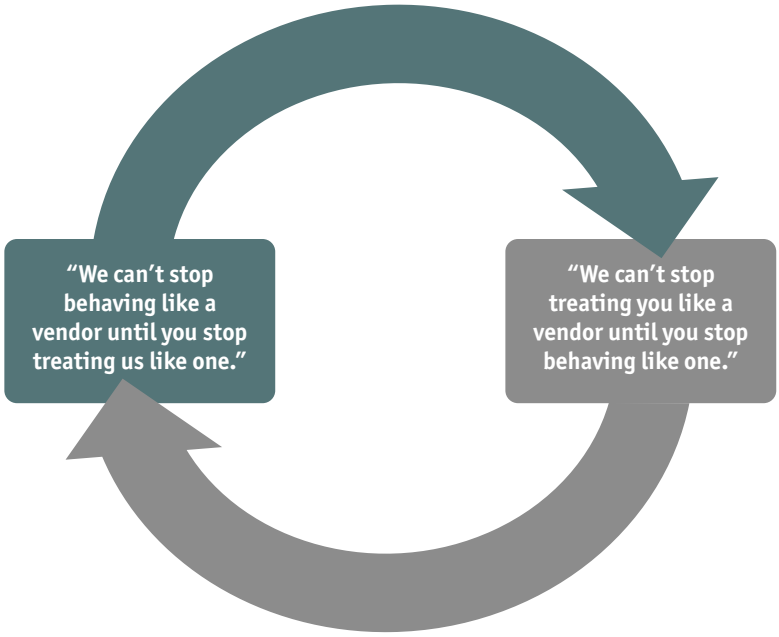


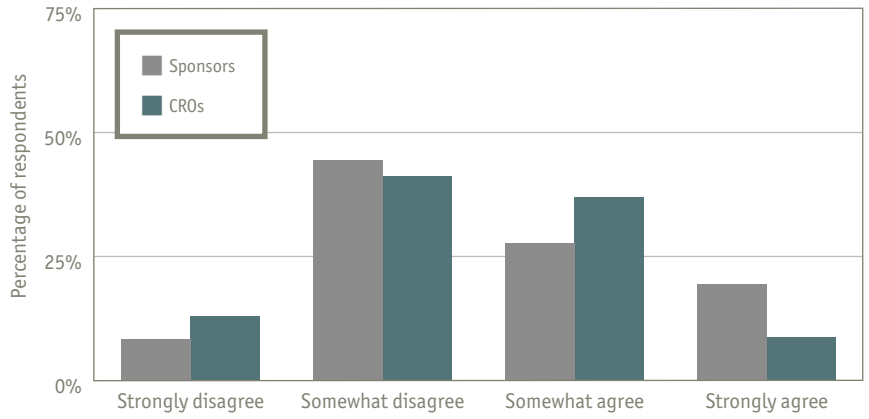
Figure 3

Characteristics of *least* successful Sponsor–CRO partnerships	Characteristics of *most* successful Sponsor–CRO partnerships
■ Both sides have unclear and unrealistic expectations of one another	■ Differences (in priorities, business models, etc.) are acknowledged and jointly managed
■ A mindset of "You work for us / we work for you" prevails	■ A mindset of "We are all colleagues" prevails
■ CROs have limited visibility into Sponsor development plans and timelines	■ Sponsors provide a high degree of transparency to CROs regarding development pipeline and plans, enabling more efficient resource deployment and management by CROs
■ Lack of clarity and alignment around policies and procedures; lack of clearly defined and differentiated roles and responsibilities	■ Processes, policies, and procedures are clearly defined and well-integrated; individuals from both companies work together seamlessly, as if part of the same organization
■ Work is either micromanaged by Sponsors or "thrown over the fence" to CROs	■ Roles and responsibilities for execution and oversight are clearly distinguished
■ Problems are often not addressed until they metastasize; finger-pointing and defensiveness are common	■ Potential problems are spotted and addressed early; both sides explore root causes and develop potential solutions together

Table 5

Tendency at Sponsors to micro-manage CROs

Extent to which Sponsors tend to over-specify requirements and procedures, and micromanage outsourced clinical trials



Graph 24

- It is not surprising that CROs report that their Sponsors tend to over-specify requirements and generally micromanage their work — this is a general lament heard from most outsourcing service providers in every industry. It is quite interesting, however, that individuals at *Sponsors* report that their own organizations are too heavy handed. Many Sponsor organizations have instructed their clinical teams to "trust but verify" — though few have formally defined what this entails in practice.
- Part of the trust problem is the reality that Sponsors are ultimately responsible for clinical trials. While regulators have begun scrutinizing CROs more closely, and holding them accountable alongside Sponsors (such as the FDA investigation of PPS Clinical Research), Sponsors still bear primary responsibility. The distinction between the team carrying out the work (operating under the pressure of timeline and cost targets) and the team ultimately responsible for quality and accuracy creates a gap in incentives that is felt very strongly at Sponsors. Continued changes in regulatory practices that hold CROs accountable have the potential to contribute to better aligning motivations and incentives. In the meantime, Sponsors and CROs can foster increased trust by structuring contracts in a way that creates shared liability for regulatory action.
- Even when the gap between incentives is narrowed, the "trust but verify" model is hampered because individuals at Sponsors generally lack a clear model and guidelines for how to effectively oversee a trial, without delving into the details as they have in the past. Most Sponsors have standard operating

(*cont. from previous page*)

What if the percentage of faulty or problematic trip reports was small (say 5 – 10%), would the Sponsor be able to spot a problem? Operations personnel were concerned that reviewing, in detail, 20% of all trip reports could be a very time consuming task that duplicated what CROs were supposed to be doing, without adding substantially more value.

The team realized they needed to think differently about the problem. The original purpose of reviewing trip reports was to identify challenges either with a site or with a CRA, and determine how best to address those challenges before they adversely impacted patients and/or the scientific validity of the trial. With CROs reviewing 100% of trip reports, they had an initial filter in place. So, they developed a formula for identifying which site and CROs were most at risk (based largely on past experience with each) and focused additional Sponsor review in those areas. As a result, they were able to substantially reduce the work conducted by Sponsor teams, increase the likelihood that a second review would spot any problems, and enhance the trust between the partners (as individuals at the CROs no longer felt their Sponsor was arbitrarily looking over their shoulder).

We were struck during interviews with Sponsors by how often they expressed disappointment with actions by CRO partners that were clearly rational, self-interested behavior.

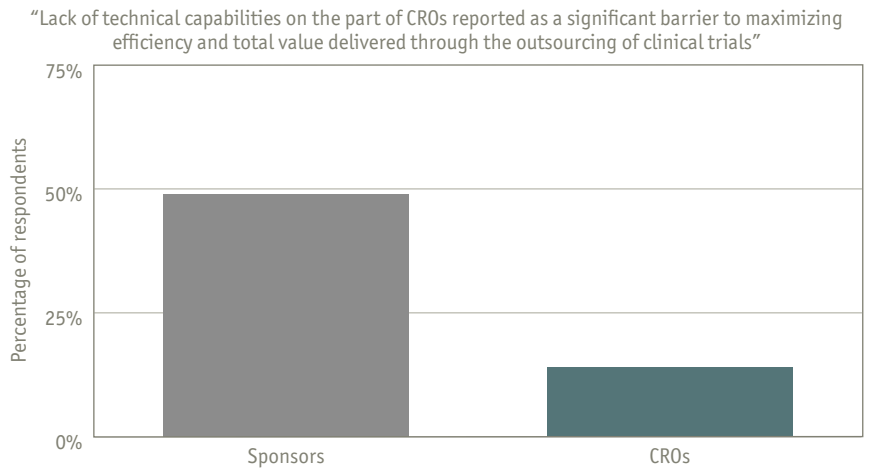
procedures (SOPs) that prescribe in great detail the actions individuals must take when conducting a trial, but lack any kind of clear, detailed procedures for managing/overseeing a third party who is executing a trial. In moving to a model where CROs conduct many trial activities (either following Sponsor SOPs or their own), individuals at Sponsors have been confronted with a tremendous challenge. How can they effectively verify CROs have done what is needed, without constantly looking over their shoulders and often redoing a very substantial portion of their work? This is a question many Sponsor organizations have not answered, and so individuals (absent any other solution) have defaulted to micro-management.

- To get out of the trap, Sponsors need to sit down with their CRO partners to scrutinize the SOPs related to all aspects of their joint work and ask two questions: (1) What is the purpose of this SOP (i.e., what problem was the SOP designed to solve for?); and (2) How might Sponsor personnel ensure that desired objectives are achieved, without requiring adherence to the specific SOP? Partners who have gone through this exercise have found it time-consuming, challenging, and (ultimately) incredibly beneficial. By looking at SOPs through these two lenses, partners are able to streamline activities and reduce micro-management while, at the same time, developing innovative new ways to ensure not only increased efficiency, but also improved quality and reduced risk.

Lack of alignment between Sponsors' expectations and CRO capabilities

- Our data indicate a significant gap between Sponsor perceptions of CRO capabilities, and CRO self-perceptions. More than three times as many Sponsor respondents perceive a lack of technical capabilities on the part of CRO staff as a problem than do CRO respondents.
- Interviews with Sponsors and CROs, as well as our experience working with both sides, suggest that the gap noted above is exacerbated by unrealistic expectations that Sponsors have about what "partnerships" or "alliances" with CROs can deliver. A strategic relationship or "partnership" with a CRO does not mean that the CRO will be single-mindedly focused on nothing but a Sponsor's success. That CRO will still have other customers (some of which may be "partners" too), and will still have an obligation to deliver profits to shareholders (private equity investors, etc.). This is obvious, of course, but we were struck during interviews with Sponsors by how often they expressed disappointment with actions by CRO partners that were clearly rational, self-interested behavior.

Degree to which Sponsors and CROs report lack of CRO technical capability as a barrier to realizing more value



Graph 25

More than three times as many Sponsor respondents perceive a lack of technical capabilities on the part of CRO staff as a problem than do CRO respondents.

- No partnership is sustainable if it rests on an expectation that either side will repeatedly sacrifice its own interests for the good of its partner. Instead, partners need to re-think the incentives (financial, and otherwise) and constraints that defined their relationship in the past, and then eliminate those factors that inevitably encourage short-term focused and opportunistic behavior. Likewise, partners need to implement different systems and incentives that enable new ways of working together, such that new benefits and greater long-term value are created for both sides.
- More "strategic" (versus "transactional") relationships with CROs can indeed deliver substantial benefits. But as noted throughout this report, such relationships necessitate significant investment of time and effort to build and maintain. Unfortunately, many Sponsors and CROs underestimate the magnitude of investment and change required, and thus set themselves up for inevitable disappointment.

	Transactional Relationships	Strategic Relationships
Strategy	Our strategy dictates how we interact with the other side. Neither side understands nor cares about the other's strategic priorities and drivers.	We regularly consider opportunities to leverage the assets and capabilities of our partner as an input to shaping our strategy. We actively seek to align our strategies.
Governance	No investment in joint governance; collaboration is ad hoc and situational.	Both sides invest in joint governance to ensure that opportunities for collaboration are identified; that collaboration is efficient; and that there is accountability across organizations to abide by defined rules of engagement.
Decision making	Maximize unilateral control. Plan and make decisions independently, without consideration for impact on partner.	Clearly define areas for shared decision making and joint planning; commit that we each will *not* make decisions that materially impact our partner without *first* consulting them.
Communication	Communication is limited. By default, information is not shared. Perceptions of inconsistent/mixed messages are common, which undermines trust.	Maximize transparency. By default, information is shared. Communication is well coordinated and consistent, which builds trust and confidence.
Mindset	Zero-sum mindset — More for them is less for us, and vice versa; therefore we need to focus on *claiming* value.	Joint gain mindset – We will maximize value for ourselves if we each focus on *creating* new value; we are committed to mutual success.
Interactions	Each side acts to maximize value for itself in every transaction, without consideration for impact to partner, or likely impact on ability to collaborate on future opportunities.	Each partner is willing to sacrifice some amount of value in specific situations to help the other side, based on a belief that this will encourage investment and enable collaboration which in turn will maximize long-term value for *both* partners.
Trust	Low levels of trust. Suspicions about the intentions of the other side are prevalent.	High levels of trust. Confidence that partner will consider our interests when they make decisions and take action, and that they are committed to *shared* success.
Differences and Conflict	Differences are not well understood, and lead to misunderstandings, friction, and conflict. Small conflicts often metastasize.	Partners invest in understanding their differences, which they leverage as a source of learning and innovation. Formal mechanisms ensure efficient and collaborative resolution of conflicts.

Table 6

Part Five

Best practices for successful Sponsor-CRO partnerships

Sponsors without a formal process to monitor trial progress are more than twice as likely to have their trials run over budget or timelines than Sponsors with such a formal process.

Realizing the potential value of Sponsor-CRO relationships requires a different approach

- In this section, we explore six key practices that characterize top-performing Sponsor-CRO partnerships.
  1. Implementation of a formal process and tools for systematically managing scope and budgets of outsourced trials
  2. Implementation of a formal process designed to facilitate identification and implementation of innovation opportunities
  3. Redesign of processes to enable greater transparency
  4. Development of a robust, multi-level governance structure
  5. Implementation of a two-way, balanced scorecard
  6. Proactive focus on change management

Sponsors with the lowest incidence of delayed and/or over budget trials (top quartile) are...	Sponsors that report that trials conducted with CROs are faster and more cost effective than those done in-house are...
Twice as likely to have a formal process for monitoring trial progress against contracted budget and scope	30% more likely to provide CROs with a high degree of visibility into their development pipelines and future plans
Four times more likely to report their CROs delivered innovation	Four times more likely to employ two-way, balanced scorecards
...when compared to Sponsors with the highest incidence of delayed and/or over budget trials (bottom quartile)	**...when compared to Sponsors that report that trials conducted with CROs are slower and/or more expensive than those done in-house**

Table 7

1. Implementation of a formal process and tools for systematically managing scope and budget

- Given the high cost of clinical trials and the dramatic revenue impact of increasing speed to market of new medicines, it is cause for concern that 47% of Sponsors have no formal process for monitoring trial progress against the contracted budget and scope or for resolving scope changes. Sponsors without these processes are more than twice as likely to have their trials run over budget or timelines than Sponsors with a formal process. Our interviews further revealed that of the processes that do exist, many are rudimentary; they rely on inaccurate data, and typically involve discussions and action only *after* budgets or scope of effort have been exceeded.

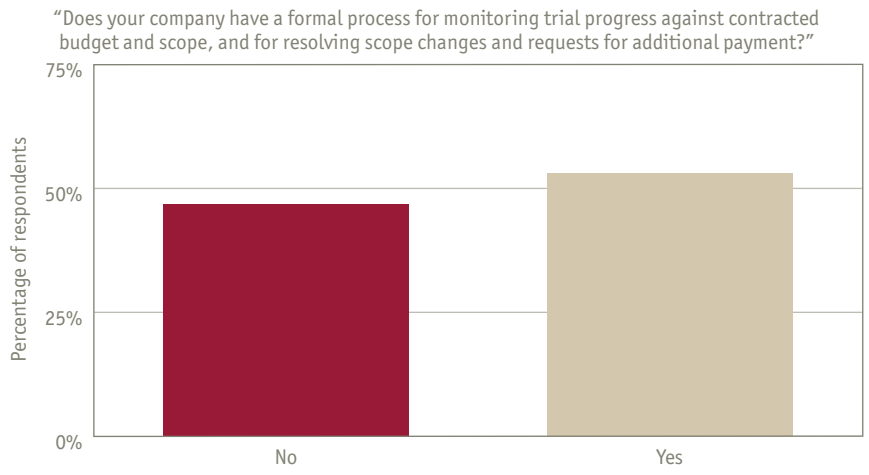
Sponsors that lack a formal process to monitor trial progress against contracted budget and scope are...	Sponsors that have a formal process to monitor trial progress against the contracted budget and scope are...
More than twice as likely to be report that their outsourced studies are significantly delayed and/or over budget	30% more likely to report that outsourced studies are either completed on time (and at or under budget) or only somewhat delayed (and/or over budget) versus significantly delayed (and/or over budget)
Twice as likely to report that they *do not know* whether outsourced trials are completed faster, the same, or slower than in house trials	Three times as likely to report that outsourced trials to are completed more quickly, and cost effectively, than in house trials
...when compared to Sponsors that have such a formal process	**...when compared to Sponsors that lack such a formal process**

Table 8

> "I know we do a lot of change orders. I don't track them. I don't think anyone does. We leave it to the Operations team to let us know if something is not correct. That needs to change."
>
> — Head of Contract Management, Global Pharmaceutical Company

- It is extremely difficult to manage a complex project without a clear plan and reliable data about progress against that plan. Rigorous tracking, reporting, and joint review of study progress and costs against plans and budgets are essential to increasing the percentage of clinical trials completed on time and within budget (see Graph 27).

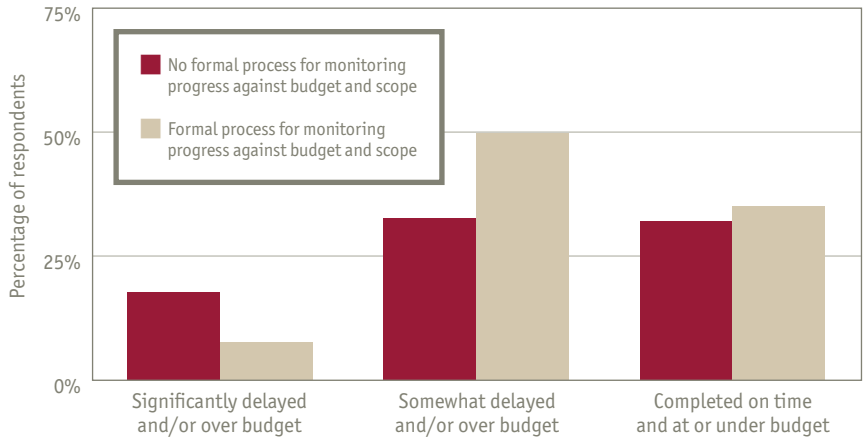
Prevalence of formal processes for monitoring trial progress against contracted budget and scope, and for resolving scope changes — per Sponsors



Graph 26

> "Our CRO partners need to reduce the number of change orders . . . we need to simplify our bid grid(s) and our specifications . . . success will require a lot of change on both sides."
>
> — Head of Procurement, Global Pharmaceutical Company

A formal process for monitoring progress against budget and scope is correlated with sponsors reporting fewer delayed and/or over budget trials



Graph 27

- Regular joint reviews of progress against budgets create opportunities for Sponsors and CROs to identify and address unforeseen difficulties early (before they cause major delays or cost increases) and to do so collaboratively. Unfortunately, many Sponsors and their CRO partners discuss delays and increased costs only when they have metastasized into major problems.
- In addition to introducing mechanisms for more disciplined scope management, Sponsors and CROs can substantially reduce the incidence of overruns by defining more realistic timelines and budgets in the first place. All too often, Sponsors and CROs collude (not deliberately, of course) to develop a budget and timelines that no one actually really expects to meet. (They may hope to do so — but that's very different.)
- Breaking this cycle requires that Sponsors and CROs recognize the structure of this dysfunctional feedback loop, and move beyond being frustrated by the other side's actions, and recognize that only *joint* action can break the cycle. Both sides need to work together to improve the process by which clinical trial timelines and budgets are developed and managed. And Sponsors need to track which CROs deliver studies at (or close to) original timelines and budgets, and which CROs regularly submit overly optimistic proposals and then fail to deliver. By doing so, Sponsors can award new studies to those CROs who have a proven track record of success, and ensure they do not reward (unintentionally) those CROs that make unrealistic bids.
- Changes to the way partners set and then monitor the scope of a trial can have dramatic impacts on final costs. If through more rigorous scope management

programs, CROs and Sponsors were able to reduce the time required per phase of their clinical trials by just 10%, they could realize an estimated 5% reduction in clinical costs, and an even larger reduction in total trial costs (see Figure 4).[27]

> "My concern is that even a partnership won't change the cycle. The incentives to underbid and underscope are very strong."
>
> — Account Manager, Global CRO

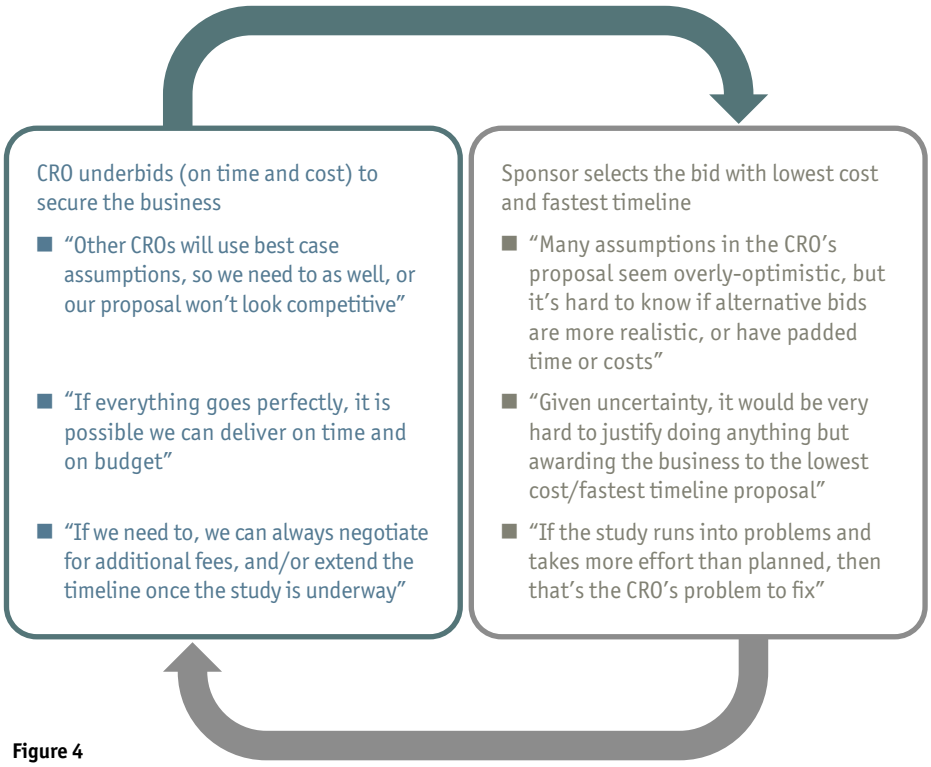
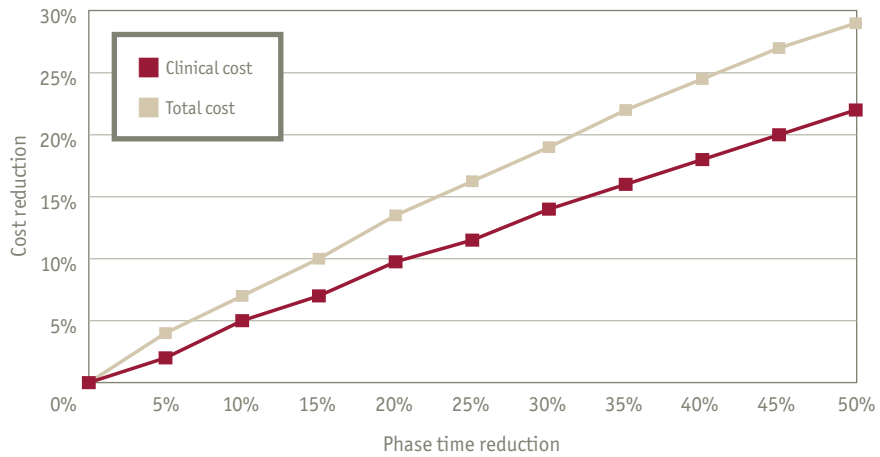


Figure 4

Cost reductions from simultaneous percentage decreases in all Phase lengths[27]



Graph 28

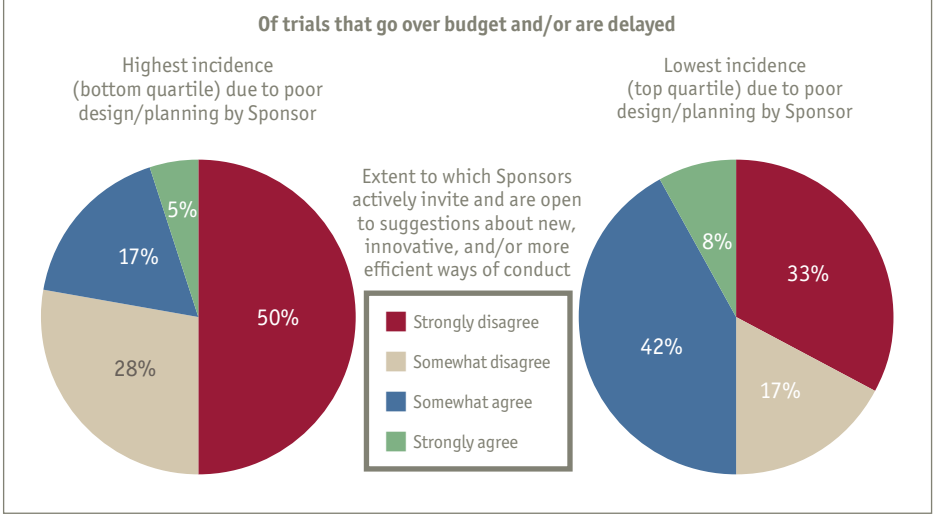
Sponsors with the lowest incidence of delayed and/or over budget trials were more than four times as likely to report that their CROs had delivered innovation compared to Sponsors with the highest incidence of delayed and/or over budget trials.

2. Implementation of a formal process designed to facilitate identification and implementation of innovation opportunities

- As discussed in Part Four of this study, while Sponsors consistently list a desire for greater innovation as one reason for entering strategic partnerships with CROs, not a single Sponsor in this study reported that they have been able to drive significant innovation through their relationship with a CRO (see Graph 19 on page 22). Sponsors that report fewer delayed and/or over budget trials, however, are consistently more likely to have worked with their CROs to develop and implement innovative approaches. In fact, Sponsors with the lowest incidence of delayed and/or over budget trials were more than four times as likely to report that their CROs had delivered innovation compared to Sponsors with the highest incidence of delayed and/or over budget trials.
- Our research and experience indicates that a few conditions (which are not currently prevalent in Sponsor-CRO relationships) are necessary to enable innovation in any commercial relationship:
  - A high degree of information sharing
  - A willingness to invest (time, effort, resources)
  - A tolerance for failure
  - A high degree of respect for different perspectives

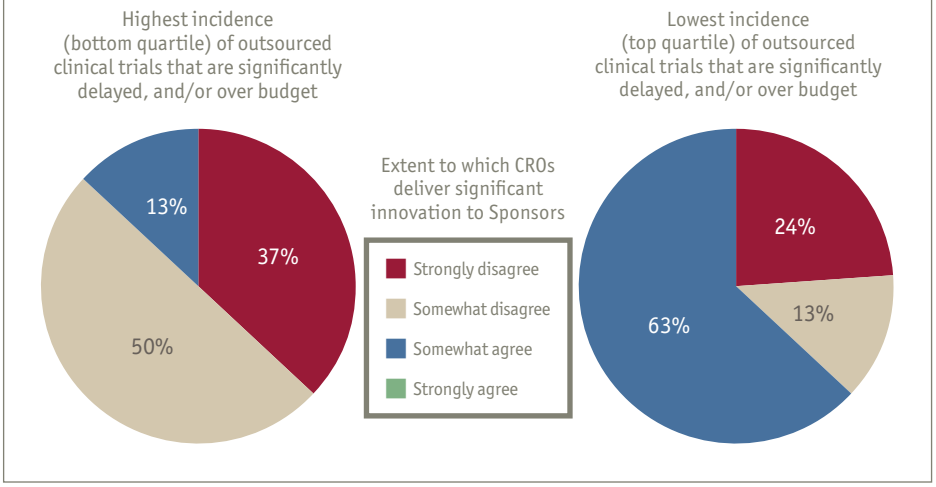
  plus
  - Clearly defined objectives related to innovation
  - Metrics by which to assess progress toward and attainment of innovation objectives
  - Incentives aligned to encourage and reward innovation

A collaborative innovation process is correlated with fewer delayed or over budget trials due to poor design/planning



Graph 29

CRO delivery of innovation to Sponsors is correlated with Sponsors reporting fewer trials that are delayed and/or over budget

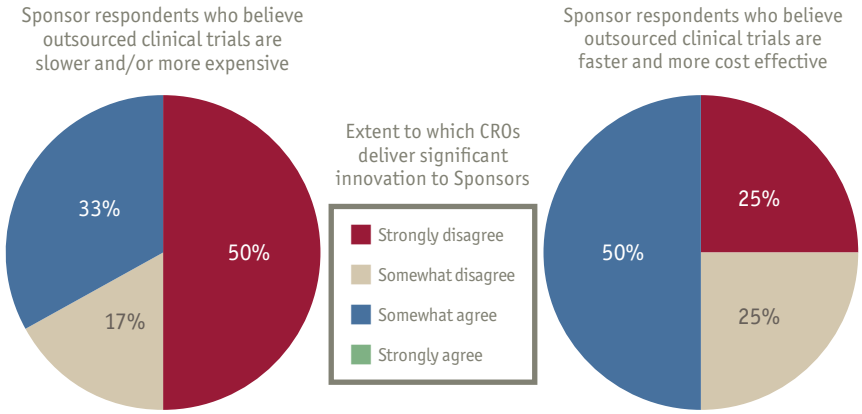


Graph 30

> "I remember an indication where we were sharing a lot of responsibility with our CRO. One of the monitors came to me and said, 'I've been thinking about the study design and I have a concern about how we're collecting the symptom data.' I listened and talked to our statistician. We even made a change based on his recommendation. I like that attitude — not being afraid of new ideas and offering solutions."
>
> — Director, Clinical Science, Mid-Sized Pharmaceutical Company

> "If [our Sponsors] would just engage us a few weeks earlier, I'm talking two or three, it would have a huge impact in our ability to plan and execute."
>
> — Head of Strategic Accounts, Global CRO

Sponsors that report CROs delivering significant innovation also report that outsourced clinical trials are faster and/or more cost efficient



Graph 31

- Leading Sponsors create these conditions by designing and implementing a collaborative approach to innovation that includes:
  - Regular communication to stakeholders in both the Sponsor and CRO organizations that clarifies (and reinforces)
    1. The goals of each organization, including how they overlap, how they conflict, and the strategy for managing any conflicts
    2. An outline of the full scope of activities and responsibilities allocated to Sponsors versus CROs
    3. The nature of innovation the partners are seeking, distinguishing continuous improvement expectations from breakthrough innovation goals
  - Regular workshops dedicated to thinking together to identify and evaluate specific opportunities, supported by a commitment from senior leaders on both sides to dedicate resources to implement ideas coming out of joint improvement and innovation workshops.
  - Revised protocol design and study planning processes — adding early engagement of CROs, along with internal peer reviews of CRO recommendations (with senior management requiring program and study teams to justify decisions to not adopt recommendations from CROs).

3. Redesign of processes to enable transparency

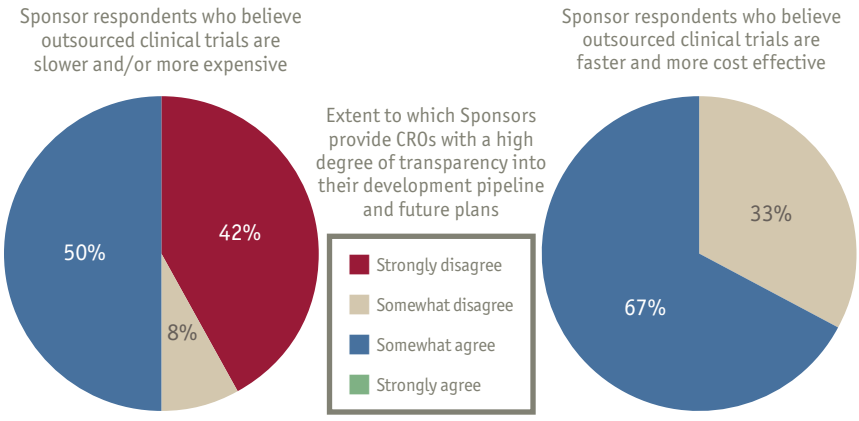
- Of Sponsors that reported that outsourced clinical trials are slower and more expensive than those conducted in-house, nearly half (42%) also reported providing CROs with very limited visibility into their development pipelines and future plans — contrasting with reports from Sponsors with faster and more cost effective outsourced trials (67% reporting a high degree of transparency).
- A high degree of transparency into development pipelines and plans correlates so strongly with faster and more cost efficient trials because such transparency provides CROs with critical information for their own internal planning. As with any business, CROs are constantly making decisions about how to best deploy their resources, when and where to increase staff, and when and where to invest in new capabilities. Getting more information earlier from key customers enables CROs to do so more effectively.
- Most CROs report having no more insight into the plans of their strategic partners than transactional clients. Those CROs who do gain insight into the plans of one or more strategic partners, are able to take that data into account and make plans that are more likely to ensure they have the right resources available and ready to go if and when their partner(s) makes a decision to move forward with a new program or study.
- Despite the advantages of sharing more information about development plans with CROs, many Sponsors hesitate to do so. Sponsors have significant, and legitimate, concerns about the risks of engaging in pipeline discussions

Most CROs report having no more insight into the plans of their strategic partners than with their transactional clients.

Sponsors that report providing CROs with a high degree of transparency into their development pipelines are...
Twice as likely to report that outsourced trials are completed more quickly and cost effectively than those conducted in house
...when compared to Sponsors that do not report providing CROs with such transparency

Table 9

Providing CROs with a high degree of transparency into development pipelines is correlated with Sponsors reporting that outsourced trials are faster and more cost efficient than in-house



Graph 32

with their CRO partners. Rather than deciding not to share much advance information about their development pipeline (as many Sponsors do), our experience suggests that Sponsors are better off sharing more information, but doing so with a clear focus on possible risks and how to mitigate them.

Sponsor concern	Advice for Sponsors on how to mitigate the risk
Transparency might actually contribute to CROs making unwise decisions, and ultimately hurt relationships with CROs CROs might develop unrealistic expectations about the likelihood that a trial will happen (and that it will be awarded to them), make plans and investments with that in mind, and feel deceived or mistreated if something changes.	■ Frame pipeline discussions in a way that manages CRO expectations. Be explicit about best current estimates of the probability that a program or study will move forward, and if so when, along with some indication of confidence levels in those estimates. ■ Provide regular, rolling updates on plans as events unfold, and as new information enables more accurate forecasting.
CROs may turn portfolio review and planning meetings into sales pitch opportunities CROs may see meetings where Sponsor pipeline data and plans are shared as a great opportunity to convince Sponsors that certain programs or studies should be awarded to them. Consciously or not, CROs may try to leverage such discussions to circumvent Sponsor bidding and award processes. If this happens, the resulting conversations will be frustrating and inefficient for Sponsors (and potentially for CROs as well) and will fail to yield any benefit.	■ While there is a real risk that this can occur, it is quite manageable with disciplined meeting design and pre-meeting communication. Be clear and explicit about the purpose of such conversations, and communicate clear ground-rules to CROs. For example, any attempts to influence or engage in conversations about award of work will not be tolerated; but any and all questions that could enable a CRO to plan and better manage their business (so they are better positioned to support any future business that may be awarded to them) are welcome. Doing this effectively requires that pipeline and planning discussions be clearly and explicitly separated from conversations related to exploring and evaluating CRO capabilities and bids, and determining how to award work. Sponsors and CROs should jointly discuss and agree upon who from each company should participate in such discussion in light of the objectives and expectations for these conversations.
Confidential information may be leaked CRO staff might (deliberately, or far more likely inadvertently) share confidential information with competitors, investors, or others that could undermine Sponsor strategies, or create legal risks for Sponsors.	■ Communicate concrete expectations regarding confidentiality and establish clear protocols to protect sensitive information. Consider providing only hard copies of materials (if any information needs to be distributed, versus simply shared orally), and prominently mark each page as "Not to be copied or distributed." Require individuals to formally "check out" and sign for any sensitive information to which they need access. And, in addition to communicating clear expectations and procedures for dealing with confidential information, explain why these procedures exist, and the potential consequences of failing to strictly follow them.

Table 10

4. Development of a robust, multi-level governance structure

- Strategic partnerships between Sponsors and CROs require robust governance: mechanisms to ensure that important decisions are identified; that optimal decisions are made (based on involvement by the right people, with access to relevant and accurate data); that accountability exists to ensure important decisions are effectively implemented; and that problems can be quickly identified and escalated to the right parties for efficient and effective resolution.
- Through this study, we found that surprisingly few Sponsors have implemented fully effective joint governance structures with their CRO partners that comprise coordinated management and oversight at each level of their relationship —from individual studies, to country-level monitoring and oversight, to overall program management (appropriately aligned to commercialization strategy), to cross-program governance of the global Sponsor-CRO relationship.
- Of course, there is no "one size fits all" governance structure appropriate to every Sponsor-CRO partnership. That said, the illustrative structure below serves to highlight many of the key design points that need to be addressed for governance of any strategic Sponsor-CRO relationship.

Effective governance requires much more than simply defining governance committees and membership.

> "Our companies are not organized in the same way. [The Sponsor] is structured by regions, we are structure by functions. I'm not quite sure how we figure out who needs to be involved in governance. I know we need to figure it out, though."
>
> — Strategic Account Manager, Global CRO

Illustrative joint governance structure

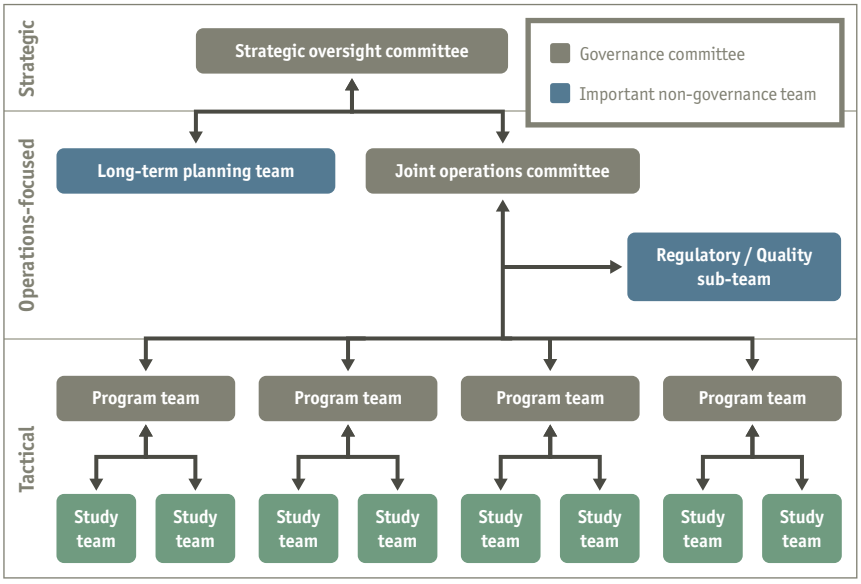


Figure 5

> "If we want to make this a strategic partnership, that means we need to be talking about the work we're doing across trials. We need a forum for escalation and we need a place where we think about and take action on cross-trial process improvement efforts."
>
> — VP, Clinical Operations, Global Pharmaceutical Company

- Effective governance requires much more than simply defining governance committees and membership. Equally essential are mechanisms and tools for the following:
  - Data gathering and analysis required to make wise decisions.
  - Roles and responsibilities for making and implementing decisions are clearly defined, and structured to minimize common decision-making biases.
  - Measurement systems are in place to track implementation of decisions, and their consequences (to enable continuous improvement of decision-making).
  - Incentives are in place to ensure accountability.
- In working with Sponsors and CROs to design joint, cross-study, and cross-program governance structures, we have found the following to be best practice design principles:
  - All decisions need to be made with appropriate cross-functional and cross-business unit involvement to ensure balanced, non-biased analysis.
  - Functional areas should generally own day-to-day interactions with Sponsor/CRO partners, with the governance structure providing oversight and a global perspective to enable more effective cross-functional coordination where necessary.
  - Decisions should be made at the lowest level where individuals have sufficient context and experience to be reasonably expected to arrive at good decisions, (which often means outside of a formal governance committee).
  - Each Sponsor-CRO relationship needs to be managed within the context of the broader portfolio of Sponsor-CRO (and other key clinical supplier) relationships (to avoid redundant investments, minimize conflicts, and maximize coordination and efficiency across the clinical development lifecycle).
  - Leaders at each company need to focus on evaluating the performance, challenges, and opportunities facing the *relationship*, as opposed to simply evaluating (and often simply blaming) the partner for any problems.
  - Committee membership should be designed in a way that ensures people with the right expertise are involved in making each decision, while enabling quality dialogue (i.e., not so many people involved in any one topic that meaningful conversation and debate is not possible). Each committee can and should be composed of two sets of individuals:
    1. Standing core members: Individuals whose input is required for most, if not all, decisions within the committee's purview and whose presence in all meetings provides continuity that enables smooth functioning of the committee

2. Extended members: Individuals who attend meetings and/or provide input only when something relevant to their function or expertise is under consideration

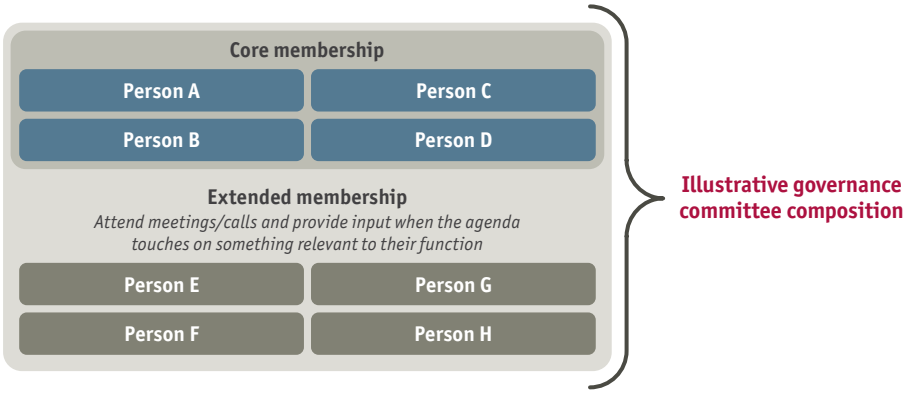


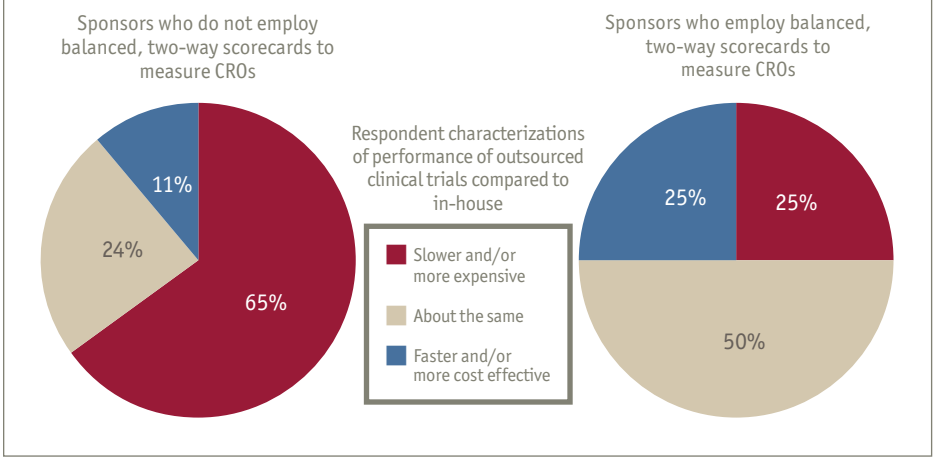
Figure 6

Sponsors that employ two-way, balanced scorecards are twice as likely to find that trials conducted with CROs are faster and more cost effective than those done in-house.

5. Implementation of a two-way, balanced scorecard

- In a recent cross-industry study of supplier relationship management programs, leading organizations consistently reported that two-way, balanced scorecards were critical for unlocking the value of their strategic supplier relationships. The survey results, and our own research, suggest such scorecards are similarly critical in the complex and high-stakes relationships between Sponsors and CROs. Sponsors that employ two-way, balanced scorecards are twice as likely to find that trials conducted with CROs are faster and more cost effective than those done in-house, yet 81% of Sponsors report that they do not use such scorecards (and, similarly, 69% of CROs report that only a few or none of their Sponsors utilize such tools).

Sponsors use of balanced, two-way scorecards is correlated with Sponsors reporting faster and/or more cost effective outsourced trials



Graph 33

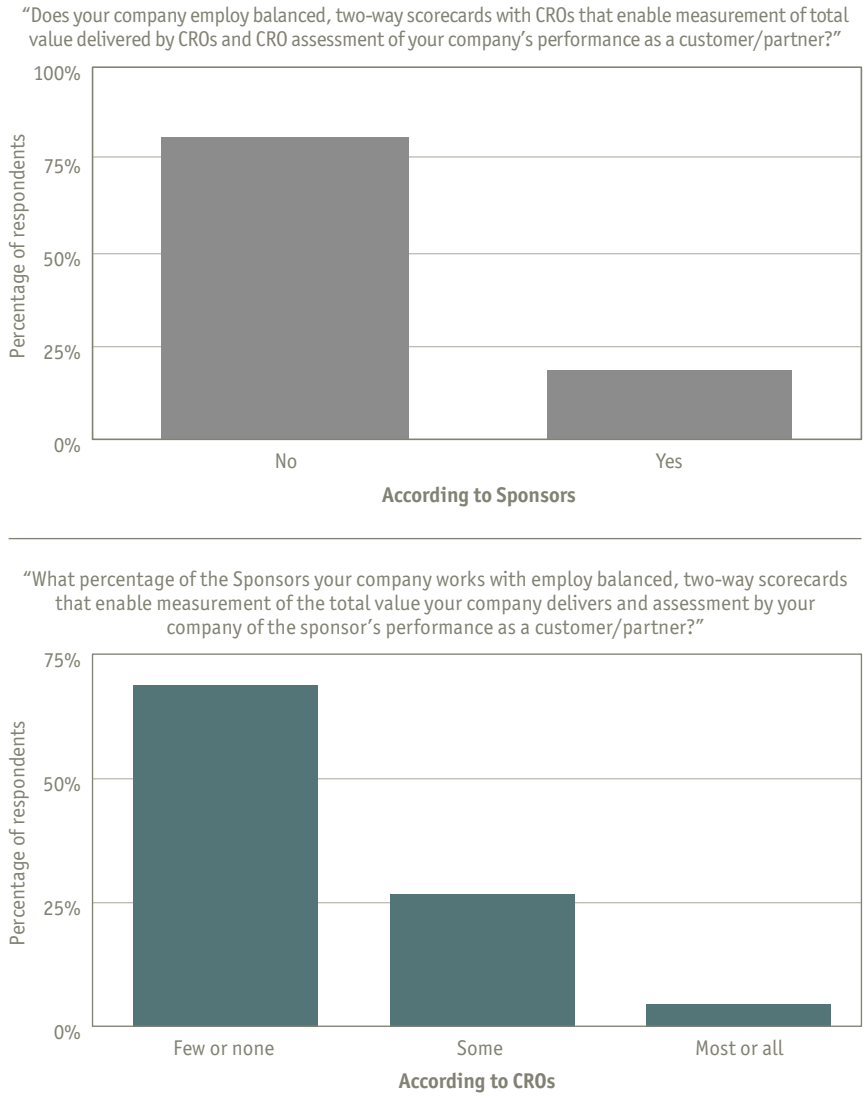
Case study: Measuring what matters

As part of the launch process for a new strategic relationship between a multi-national pharmaceutical and a leading CRO, the two companies formed a team to look at the metrics they had been using and determine what, if any, changes should be made given the new relationship.

One of the first pieces of feedback from the CRO was, "You seem very focused on first patient in, and we're concerned that the drive to get one site up and enrolling is damaging your trials." The Sponsor was understandably surprised (as this is a metric used by many pharmaceutical companies for both internal and outsourced trials). After discussion, however, they realized that the teams were so focused on that first patient that they often moved aggressively, hit the milestone, and then had to go back and rework the protocol and many operational processes — creating unnecessary churn and expense at both the Sponsor and CRO.

The solution? Balancing the first patient in with metrics regarding re-work and protocol accuracy.

Sponsor-CRO scorecards that measure total value of company performance



Graph 34

- Through our research and consulting work, we have identified a few critical guidelines for developing and using performance scorecards.

  1. **Measure what matters:** Avoid the temptation to measure too many things, or focusing on what is easy to measure. Think carefully about which measures ought to be captured at which levels of the relationship. Consider starting by looking at the data currently captured by both Sponsor (for in-house trials) and CRO (for its own purposes and for other Sponsors). Most of the important data will be on such a list, and it is just a matter of filtering

through it to identify the really critical metrics and selecting the best method of capturing them (often, Sponsors and CROs will have developed different measures for the same underlying item, and one may be more accurate and/or easier to capture than another).

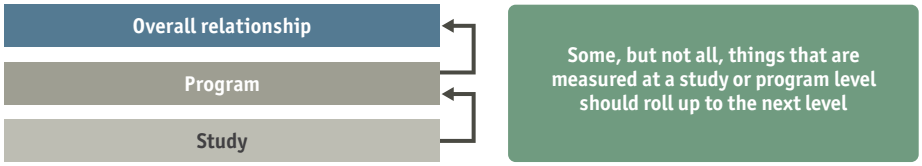


Figure 7

2. **Develop and utilize predictive measures as well as metrics of outcomes:** Though data such as cost-per-patient-enrolled and number of adverse findings in a quality audit are critically important, they provide a backward-looking picture of performance. Tracking forward-looking measures such as progress against upcoming milestones and soft metrics about the level of trust and quality of collaboration between partners provides opportunities to spot and address risk factors and prevent problems from occurring in the first place.

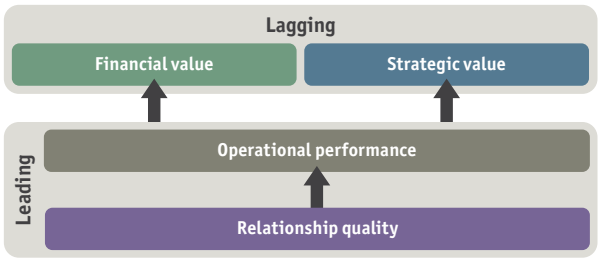


Figure 8

3. **Accept that some measures are subjective or approximate:** The purpose of metrics is to provide useful data to ground thinking and conversations about where things are working and where they need to be improved. To do this, metrics do not need to always be completely objective or precise. (As William Bruce Cameron once said — in a memorable formulation often attributed to Einstein — "Not everything that counts can be counted, and not everything that can be counted counts.") Critical dimensions of measurement (e.g., the quality of the working relationship and strategic value) by definition require dealing with individual perceptions and the application of human judgment. Metrics cannot take the place of conversations between business partners, but they can catalyze conversations (so that critical issues are addressed in a timely fashion), and ground conversations in a common fact-base, — with the ultimate objective of enabling more effective problem identification, diagnosis, and resolution, and overall performance improvement.

Metrics cannot take the place of conversations between business partners, but they can catalyze conversations (so that critical issues are addressed in a timely fashion), and ground conversations in a common fact-base.

> "We need a joint scorecard, and it is a lot of work to do it right the first time. We don't want to put more burdens on our folks. We want them to have the appropriate metrics without needing to do a lot more work. Something simple to collect, but meaningful."
>
> — Senior Vice President, Clinical Science, Global Pharmaceutical Company

4. **Ensure metrics are used within a joint performance review and continuous improvement process:** Scorecards and KPIs are not an end in and of themselves. They should be used to facilitate effective dialogue to improve individual company performance and the quality of the Sponsor-CRO collaboration. Such discussion should then lead to development of concrete remediation or improvement plans that drive measurable improvements.
5. **Use metrics collaboratively, not (only) punitively:** Use metrics to diagnose what each company has done or failed to do that may have contributed to any problems – rather than simply to assign or blame or decide whether or not to apply penalties. That is, use metrics to jointly diagnose and solve problems, and identify improvement opportunities, not simply to penalize poor performance.
6. **Select metrics that enable both Sponsors and CROs to assess the value they realize from the relationship:** In a strategic partnership, each side has a clear understanding of the other's goals for the relationship, as well as a commitment to help their partner succeed. This is a matter of enlightened self-interest. There is simply no sustainable way for a company to succeed at the expense of an important business partner. (If CRO partners lose money on the relationship or working with Sponsors is so difficult that the best employees quickly search for other assignments, then Sponsors' goals cannot be achieved in the long run either.)

Illustrative joint scorecard

Strategic value	Financial value
■ Number of programs and/or trials where the CRO was engaged before protocol design ■ Number of CRO protocol suggestions adopted ■ Number and quality of innovative new ideas provided by the CRO ■ Number of new innovations implemented	■ Budget and pricing accuracy ■ % direct-indirect spend for development ■ Direct cost per patient (per month of exposure) ■ Number of internal FTEs per study per month
Operational performance	**Relationship quality**
■ Number of protocol amendments after approval ■ Actual site activation vs. projections ■ % country regulatory packets approved at receipt ■ Actual enrollment vs. projections ■ Cycle time (last patient last visit complete to database lock to final tables and listing) ■ Routine monitoring visit and trip report timeliness ■ Expedited safety report timeliness	■ Critical issue escalation cycle time ■ Staff turnover ■ Level of trust ■ Quality of communication ■ Quality of problem-solving ■ Degree of mutual understanding

Figure 9

6. Proactive focus on change management

- In Part Four, we explored barriers to building and sustaining collaborative partnerships between Sponsors and CROs and to improving the performance of outsourced clinical trials (see Graph 10 on page 13 and Graph 11 on page 14). Overcoming these barriers requires a fundamental shift in mindset and behaviors at both CROs and Sponsors. On the CRO side, individuals accustomed to taking close direction from Sponsors must become more proactive and take on greater responsibility for delivering quality results (versus simply executing tasks). On the Sponsor side, individuals who once were responsible for execution must adopt a relationship management and oversight role — maintaining ultimate accountability for patient safety and data integrity, without direct responsibility for execution.

- To enable this kind of fundamental change, Sponsors need to clearly articulate the performance standards and outputs for which CROs will be responsible, while being more flexible about *how* a CRO will manage the work. Sponsors and CROs also need to re-think the roles of their staff and equip them with new skills and tools. Specific elements of programs to enable such a change include:

1. Clarify and redefine procedures

Given the highly-regulated nature (and life and death stakes for patients) of the Life Sciences sector, concerns about compliance lead many Sponsors to define stringent and highly prescriptive standard operating procedures (SOPs). While detailed SOPs help to ensure compliance, in an outsourced environment they can also create significant challenges:

- Constrained innovation and creativity, as CROs are required to follow highly-specified Sponsor procedures
- Confusion — leading to inefficiency and potential conflict, when CRO and Sponsor both have different SOPs for the same tasks (and these SOPs have not been rationalized or harmonized)
- Increased risk of error, when CRO staff are made to perform the same tasks in different ways, for different Sponsors (and, all too often, on different studies for the same Sponsor as well)

Sponsors and CROs therefore face the challenge of clarifying and redefining procedures in a way that ensures a Sponsor maintains its regulatory accountability, while simultaneously allowing their CRO flexibility to define its own operational procedures. One effective approach to this challenge is to agree in principle that the party who has responsibility for execution of a task should follow their own organization's SOP for that task (for the purpose of clarity, and to reduce risk). Sponsor and CRO should jointly review the end-to-end clinical trial process, looking for areas of redundancy

Sponsors and CROs also need to re-think the roles of their staff and equip them with new skills and tools.

> "We've got to focus on change management. That is the crucial element here. If we do it well, I know we will succeed. If we neglect it, this [new partnership] won't be any different from the ad hoc outsourcing we were doing before."
>
> — Clinical Operations Lead, Global Pharmaceutical Company

On the CRO side, individuals accustomed to taking close direction from Sponsors must become more proactive and take on greater responsibility for delivering quality results (versus simply executing tasks). On the Sponsor side, individuals who once were responsible for execution must adopt a relationship management and oversight role.

(deciding who will be responsible for planning and execution of tasks) as well as appropriate control points (deciding when and how Sponsor staff will review or audit work). Such an approach ensures compliance and risk are optimally managed, without unnecessary duplication of effort.

With a view of the process from beginning to end, SOPs can then be rationalized — Sponsor SOPs for tasks that will be the responsibility of their CRO can either be retired or rewritten to describe the new activities that Sponsor staff will perform to oversee the work and manage the relationship with their CRO (vs. execute the task). For example, a Sponsor SOP for site selection might be rewritten to focus on creating criteria for site selection and reviewing exception sites that do not meet the criteria. CRO staff would follow their own SOP for the process of qualifying and selecting sites (in accordance with Sponsor-defined criteria).

2. Define attractive new roles

The exercise of reviewing clinical trial processes and identifying responsibilities for planning and execution of tasks can leave Sponsor staff concerned about "what remains" of their jobs. They may perceive (rightly or wrongly) that their workload has been diminished, and will certainly notice that the nature of the work that remains is different. This often produces anxiety about whether or not they will successful, and even fear that their jobs might in jeopardy.

	Common (but problematic) approach	More effective approach
Leadership messages	Vague, high-level directives (e.g., "*We need to be more strategic*") combined with a focus on ensuring compliance, and oversight of CRO work (e.g., "*We are still ultimately accountable*")	Clear articulation of the expected responsibilities of re-defined role (e.g., strategic planning, risk management, joint corrective action), along with a compelling description of the value those activities provide to the Sponsor organization
Formal role definitions	Remain as they were prior to engaging in the collaborative partnership	Rewritten (potentially creating new titles) to reflect different responsibilities and associated necessary skills
Performance measurement	Continue to measure execution tasks, which Sponsor staff no longer directly control	Focus on *outcomes* as well as actions Sponsor staff should (and should not) take to enable CRO partners to achieve strong results on behalf of the Sponsor
Resulting perception *of Sponsor personnel* about the nature of their new role	Our role is to "police" the provider; to discover their errors or shortcomings, and ensure appropriate punitive action is taken (and by extension, the more successful our CRO is, the more redundant our role becomes)	Our role is to manage a strategic relationship — setting plans, managing risks, and removing barriers (therefore, the more successful our CRO is, the more successful we will be)

Figure 10

As (additional) clinical research activities are outsourced, individuals within Sponsor organizations need to clearly understand their new roles and the value those roles bring to the organization. Providing the necessary clarity requires redefining job descriptions, performance measures, and messages about the nature of the job, as outlined in Figure 10.

3. Develop new skills

Collaboration is ultimately about the interactions that happen between individuals at Sponsors and CROs on a daily basis. Therefore, individuals need to be equipped with the skills required to operate in a different way. In the past, the skills required of Sponsor staff related to executing clinical trial activities. In their new roles, however, Sponsor staff must develop strong oversight and relationship management skills.

When determining how to enable Sponsor staff to develop the right skills for their new roles, it is helpful to separate the required skills into two categories:

1. Analytical skills which can be developed through a variety of mechanisms, including lecture, reading, and computer-based training
2. Behavioral skills which generally require experiential learning vehicles and extensive reinforcement to ensure the skills are used even in high stakes, high stress situations (because developing these skills involves unfreezing strongly held beliefs and unconscious assumptions, introducing new ideas, then "refreezing" to make the new behaviors part of the individual's repertoire)

Collaboration is ultimately about the interactions that happen between individuals at Sponsors and CROs on a daily basis. Therefore, individuals need to be equipped with the skills required to operate in a different way.

Illustrative skills needed for Sponsor staff in oversight roles

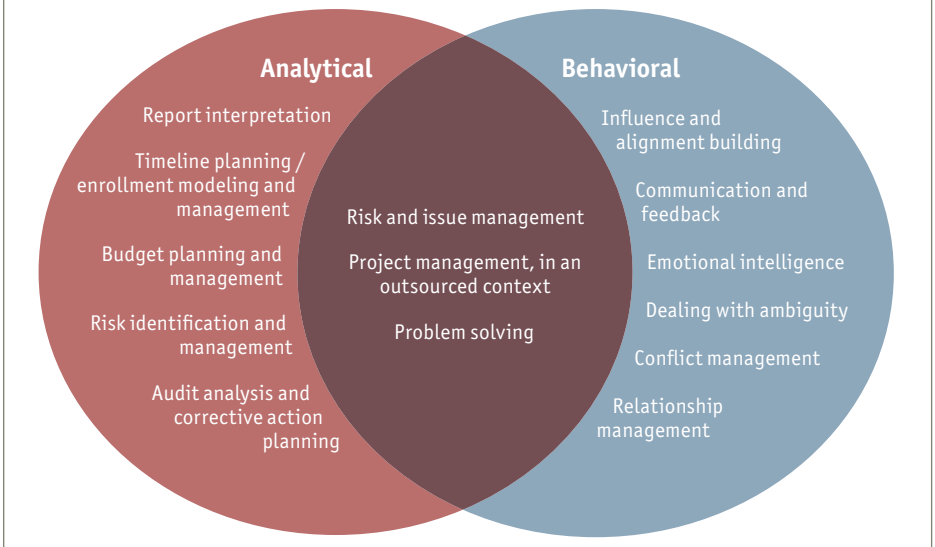


Figure 11

The most successful training and development programs span several months and incorporate multiple modes of learning: classroom training, online workshops or tutorials, intact team workshops, and consistent feedback and reinforcement from senior management.

While there is some overlap between the skills Sponsor staff need to manage studies in-house or through ad hoc CRO engagements and the above skills (which Sponsor staff need to realize the most value from a CRO partnership), there are also substantial differences. Not surprisingly, developing these skills requires a significant investment of time and resources. A set of online learning modules and/or a one-off training event is not sufficient. Individuals need time to absorb new information, become accustomed to new procedures and responsibilities, and to try out new patterns of behavior. The most successful training and development programs span several months and incorporate multiple modes of learning: classroom training, online workshops or tutorials, intact team workshops, and consistent feedback and reinforcement from senior management.

Conclusion

Sponsors that want to significantly improve the performance of their outsourced trials (in terms of patient safety, data quality, cost, and speed) need to fundamentally alter the nature of their relationships with CROs. It is not enough to simply change the contract from ad hoc to preferred supplier or to name the relationship a "strategic partnership." Sponsors and CROs face significant barriers to improving the results of their work together, including:

- Failure by Sponsors to involve CROs early or deeply enough in trial and protocol design and planning
- Lack of ability by Sponsors and CROs staff to work collaboratively as partners
- Failure by Sponsors to provide CROs sufficient visibility into their development pipelines
- Lack of standardization of protocols, procedures, tools, data formats, etc.
- Lack of investment in software tools to enable communication, management, and automation of activities
- Tendency at Sponsors to micro-manage CROs
- Lack of alignment between Sponsor expectations and CRO capabilities

Overcoming these barriers requires Sponsors and CROs to sit down *together* to make significant changes in the ways both organizations work. Doing this requires:

- Active and disciplined management of outsourced trial scope and budget
- Formal processes to facilitate the identification and implementation of innovation opportunities
- Re-designed processes that enable greater transparency
- Joint, multi-level governance
- Performance management supported by a two-way, balanced scorecard
- Substantial investment in systematic change management

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