Accelerate the Startup of Your Clinical Trials Without Sacrificing Quality

Common Pitfalls That Cause Delays and How to Avoid Them

17 June 2021

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Tufts Center for the Study of Drug Development
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Common Pitfalls that Challenge Clinical Trial Performance

Ken Getz
Director and Professor
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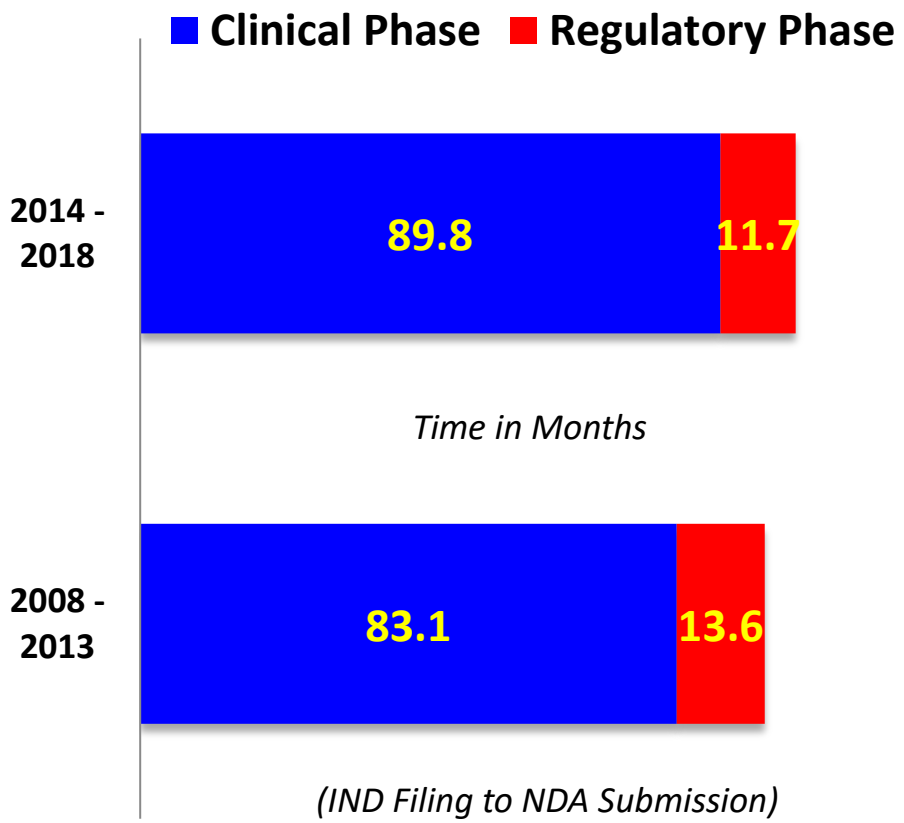
Tufts University School of Medicine

June 2021

Trends in Program and Clinical Trial Cycle Times



	Mean Clinical Trial Duration (Months)	Coefficient of Variation
Phase I		
2008-2013	13.8	1.59
2014-2018	14.8	1.51
Phase II		
2008-2013	27.1	.88
2014-2018	30.2	.85
Phase III		
2008-2013	26.8	.83
2014-2018	28.5	.75

Source: Tufts CSDD, 2020. N = 377 new drugs and biologics approved by CDER (FDA)

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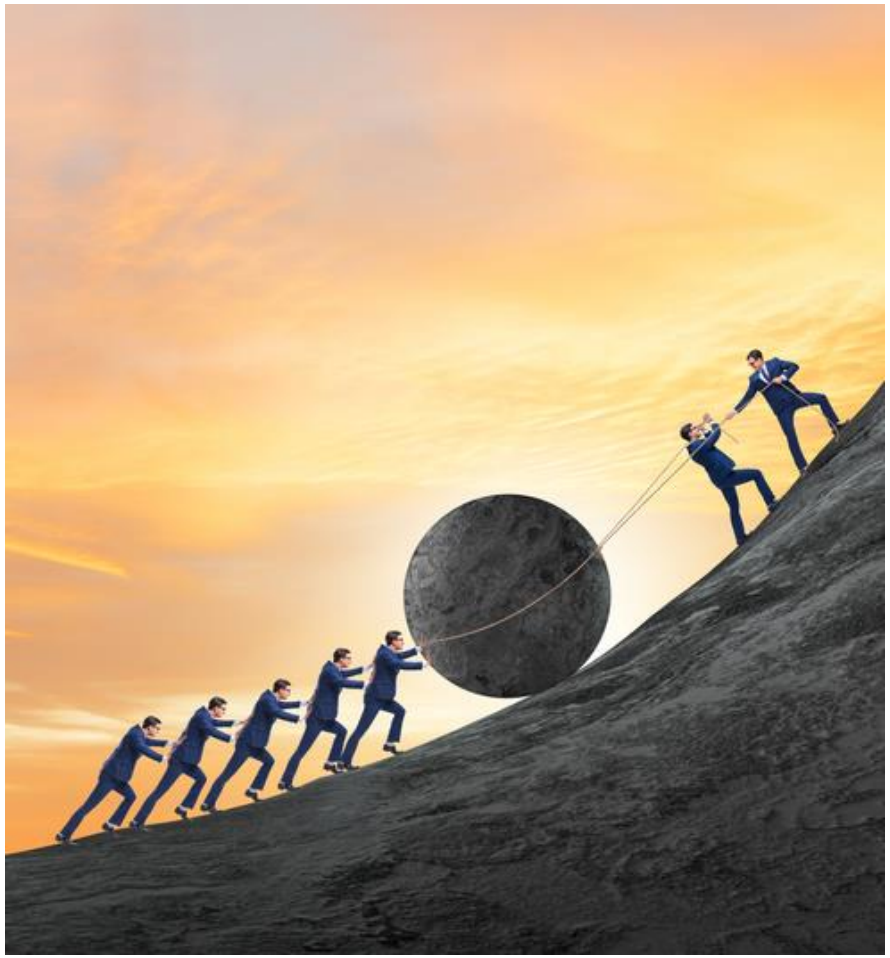
Key Drivers of Development Operating Conditions



- **Executional Complexity**
- **Hyper-Customization**
- **Operating Fragmentation**

Protocol Design Trends

Phase III Pivotal Trials *(means)*	2005	2011	2020	15-Year CAGR
Total Endpoints	7	13	22	7.9%
Total Eligibility Criteria	31	34	30	-0.2%
Total Procedures	110	187	263	5.9%
Number of Substantial Amendments	2.0	2.3	3.4	3.6%
Total Countries	6	9	15	6.3%
Total Investigative Sites	40	65	104	6.6%
Procedures per Planned Patient Visit	9	11	13	2.5%
Total Data Points	494,000	929,000	3,560,000	14.1%

Source: Tufts CSDD

Clinical Research Data

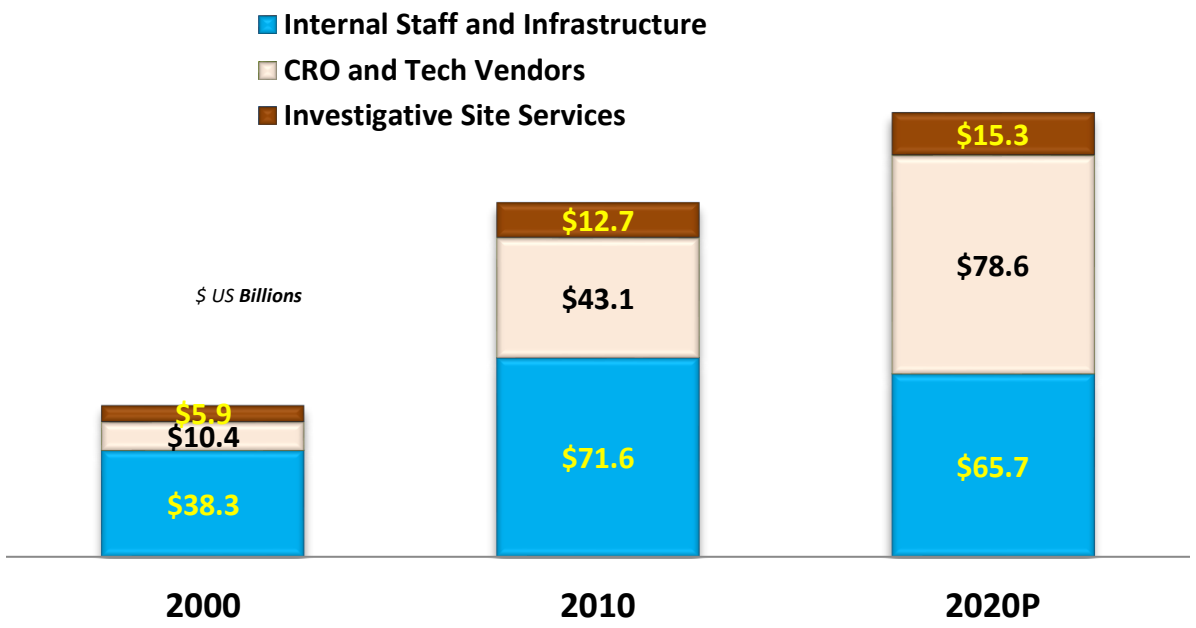
Incidence of Data Type in the Study Database

(Percent of companies reporting)	Current	Projected in 3 Years
Electronic and Paper Case Report Forms	100%	100%
Local and Central Labs	60%	65%
Smart Phones	45%	92%
Electronic Clinical Outcomes Assessments	21%	93%
Electronic Health and Medical Records	20%	67%
eSource	38%	84%
Mobile Health and Wearable Devices	29%	76%
Social Media	6%	27%

Source: Tufts CSDD/.Veeva 2019; N=282 sponsor and CRO companies; Tufts CSDD 2017 N=257 unique sponsors and CROs

The Global Landscape of Organizations

Distribution of Global R&D Spending



Primary Segments

	Number of Companies
Pharmaceutical and Biotechnology Sponsors	~4,275
Contract Research Service Providers	~3,300
Technology Services Providers	~1,600
Study Conduct Services (Investigative Sites)	~38,000

Source: EvaluatePharma; CenterWatch; William Blair & Wells Fargo Securities; TCSDD

Top Qualification Areas Assessed

Top Assessment Areas	Percent of Companies
Data privacy and protection	94.3%
Quality management systems	92.5%
Facilities management	88.7%
Computer Systems 21 CFR 11 compliance	86.8%
Document management and control	85.3%
IT quality and security	84.0%
Confidentiality	84.0%
Training	81.1%
Project management	76.4%
3rd party quality management and oversight	72.6%
Physical security procedures	71.7%
Financial stability	69.8%
Anti-corruption due diligence	59.4%

A Time-Intensive and Inefficient Process

3 – 4.5 weeks

(0.6)

6.8 – 9.8 weeks

(0.7)

7.4 – 9.2 weeks

(1.0)

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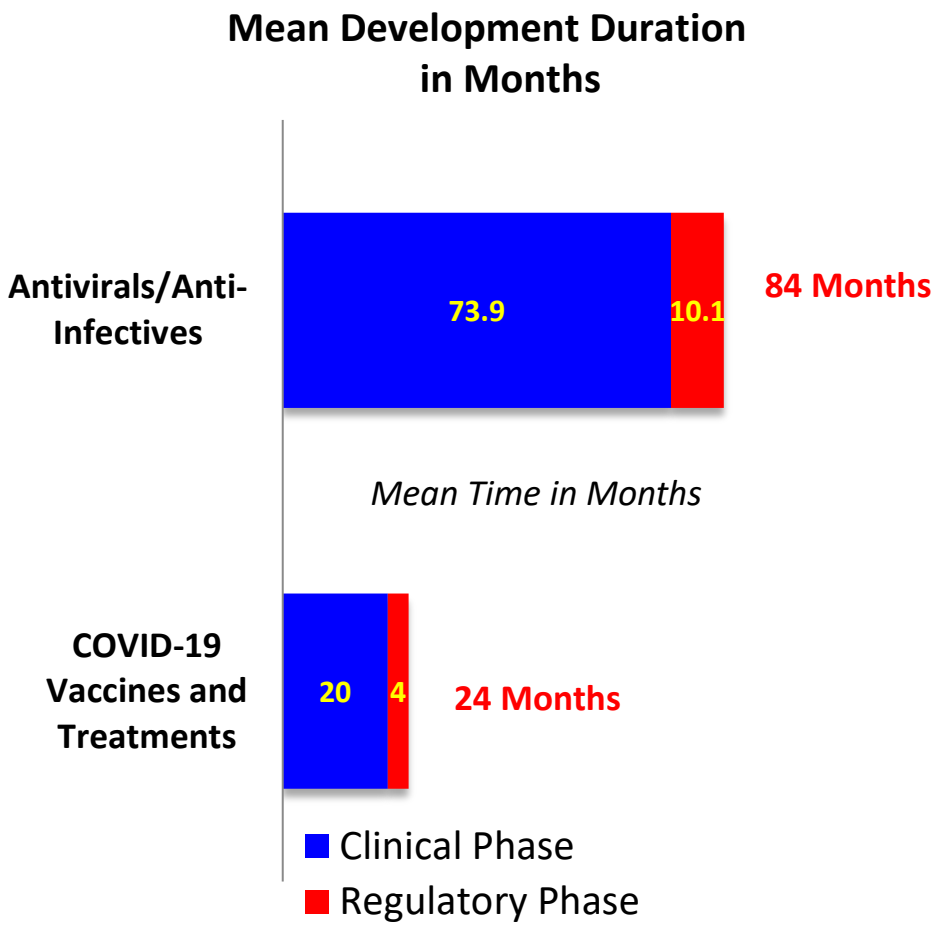
Complexity Inversely Related to Performance

Phase III Pivotal Trials	10-year Change	Significance
Study Initiation Duration (approval to FPFV)	27.2%	<.05
Study Conduct Duration (FPFV – LPLV)	36.9%	<.001
Study Closeout Duration (LPLV to DBL)	16.3%	<.05
Total Number of Substantial Amendments	113.3%	<.001
Drop-Out Rate	105.1%	<.001

Source: Tufts CSDD, 2020

‘Unprecedented’ Pandemic Response



- **Proactive and accommodating regulatory agency involvement**
- **Simultaneous and collapsed clinical trial phase activity**
- **Singularly focused, open innovation, collaboration and data-sharing**
- **Rapid mobilization of scientific and operating teams**
- **Fast deployment of remote and virtual technology solutions and advanced analytics**
- **Additional funding and resources**
- **Unusually high public visibility and media coverage**

Source: Tufts CSDD 2020

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Primary Themes from Global Investigative Sites

POSITIVES	NEGATIVES
• Excellent sponsor and regulatory responsiveness to adaptations and adjustments • Greater patient/study volunteer convenience • Increased choices for patients	• Much greater workload for site personnel • Too much uncertainty • Highly fragmented and siloed activity • Rapid roll-out of new technology requiring more training • Delays (supplies, lab kits, payments) • Increased potential for errors and mistakes

Source: Tufts CSDD 2021; In-depth Site Interviews N=43

Forecasting Sponsor Behavior

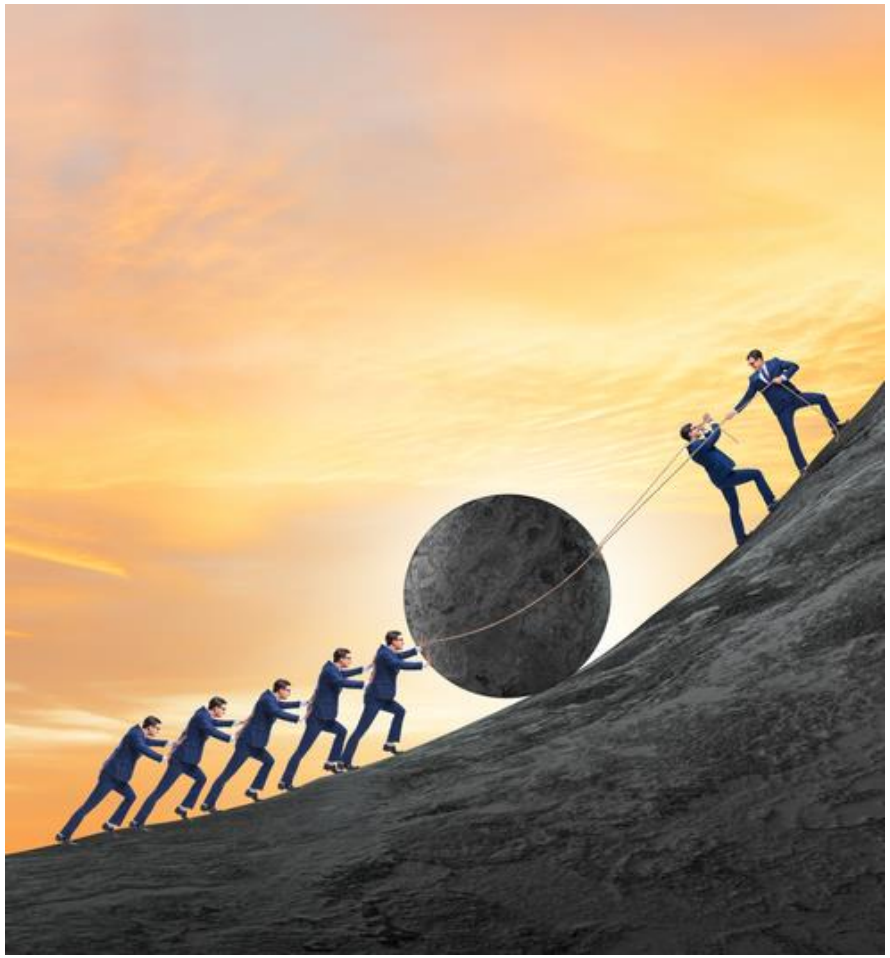
Percent report	'Used' Prior to Pandemic	Began Use During Pandemic	Anticipate 'Strong' Use Post-Pandemic
eConsent	52%	39%	63%
eSource	38%	38%	56%
Remote Monitoring	50%	36%	55%
Wearables	57%	25%	50%
Telemedicine visits	37%	58%	36%
Home visits	44%	48%	32%
Ship-to-home supplies	27%	65%	29%

Source: The Avoca Group, 2021: N=145 Sponsors and 84 CROs

Implications and Opportunities

- **Complexity and customization will continue to increase as demand for hybrid operating approaches and more patient choices rise**
- **Agile and flexible infrastructure, integrated systems, SOPS, staff allocation**
- **Consolidation and more efficient use of fixed operating elements**

Implications and Opportunities *(continued)*



- Growing use of intermediaries, open collaborations and data-sharing with more infrastructure and systems to support them
- Continued growth in data volume from diverse sources and rising demand for solutions and personnel to leverage this data
- Increased reliance on augmented clinical and operating data management and analysis (e.g. AI, RBQM and risk-mitigation)

Please use the Q&A Box to ask a question, or contact me

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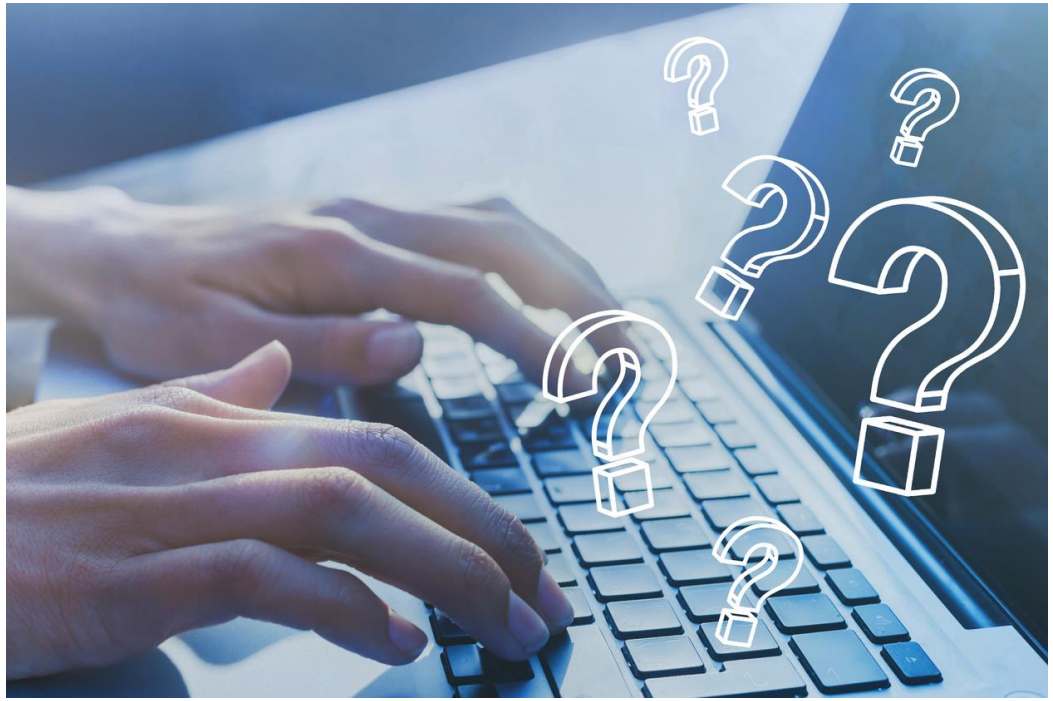

Opportunities to Avoid Pitfalls and Accelerate Timelines

Jay Turpen
Head of Client Services
Diligent Pharma, LLC

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Multiple Players in the Clinical Trial Landscape

1990s clinical research

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Multiple Players in the Clinical Trial Landscape

Today

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Multiple Players in the Clinical Trial Landscape

Today

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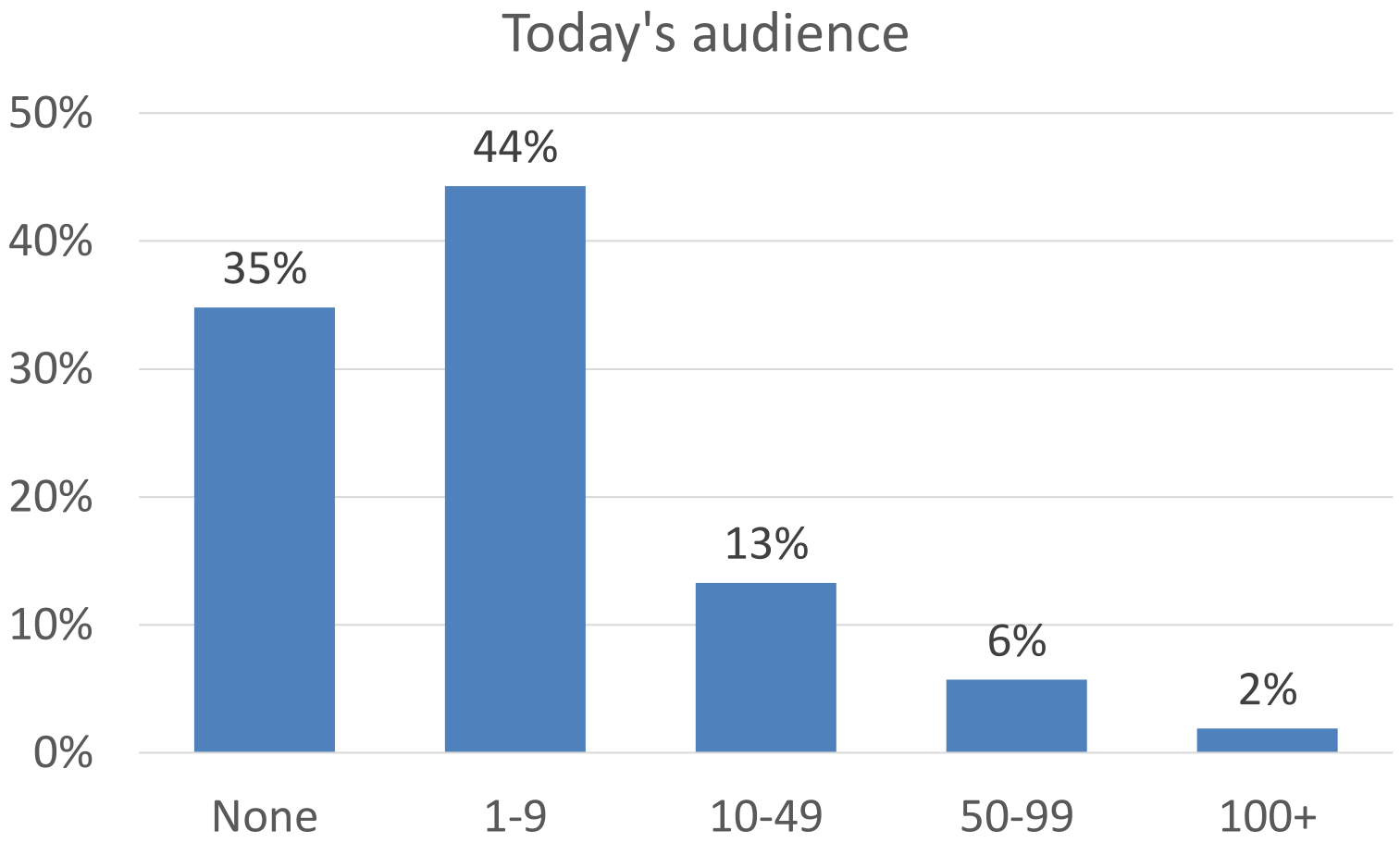
Here’s what you told us of your experience

Registration poll:
How many clinical research supplier RFIs (Requests for Information) or VQAs (Vendor Qualification Assessments) did you work on over the last 12 months?



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Pulling the team together into a system

"A system is a network of interdependent components that work together to try to accomplish a common aim of the system.
A system must have an aim. Without the aim, there is no system."

W. Edward Deming

System Thinking

Common Aims/Goals

- Maintain "Inspection Readiness" at all times during the Clinical Trial
- Accelerate to deliver unmet medical need to patients
- FPFV by _____
- 90% Investigators Activated by _____
- Enrolled Patient Demographics = Right Patients/Subgroups Enrolled
- LPET by _____
- Avoid Protocol & Process Deviations
- % Data Clean >= _____
- LPLV by _____
- DBL by ___ days after LPLV
- CSR by ___ days after DBL
- Deliver Clinical Trial with Quality, ahead of timeline and under budget

Are we effective at conveying "common aims" to all team members?

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Reactive vs Proactive Mindset

"Be proactive not reactive, for an apparently insignificant issue ignored today can spawn tomorrow's catastrophe."

Ken Poirot

Reactive vs Proactive Mindset

"Be proactive not reactive, for an apparently insignificant issue ignored today can spawn tomorrow's catastrophe."

Ken Poirot

- We are on an accelerated timeline and don't have time for all this planning.
- There are too many unknowns to build a plan.
- Let's just get stuff done.
- This worked last time, so it will work this time.

- The only way we can deliver this accelerated timeline is to have a robust plan.
- Let's make sure all the pieces fit together and team members understand their roles.
- Investment in planning upfront can help us avoid pitfalls.
- We must "Do it right the first time."

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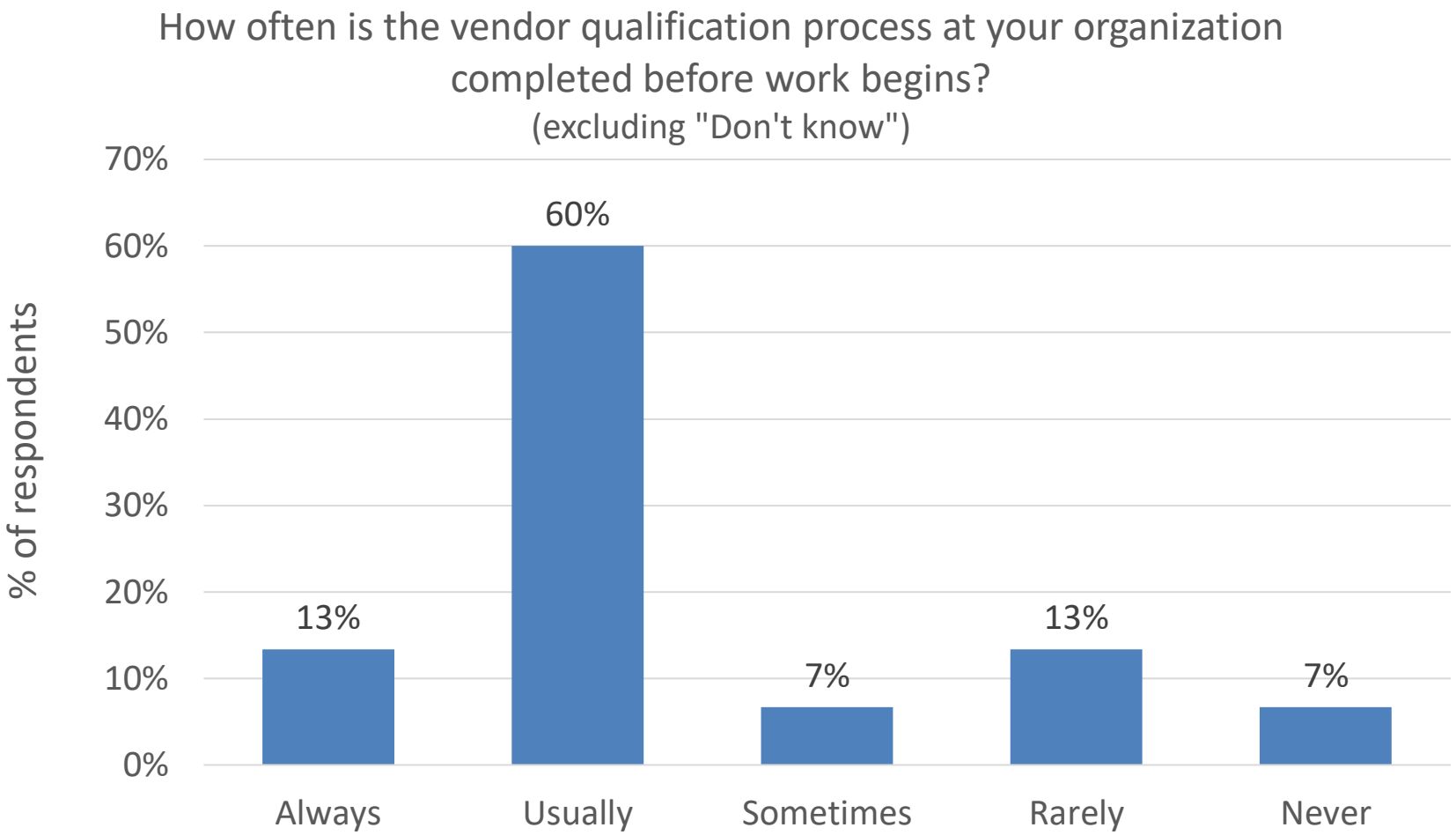
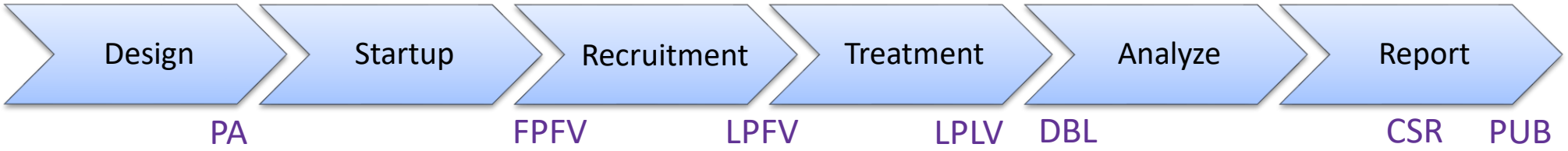
Poll question



Work Smarter Not Harder to Accelerate Timelines



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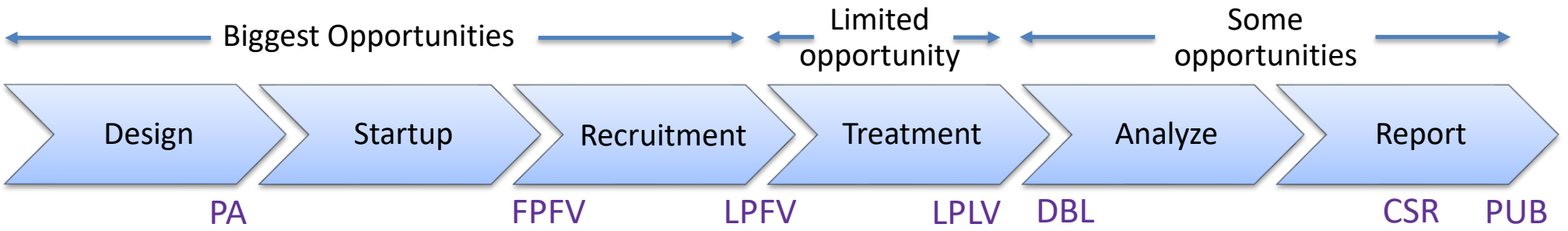

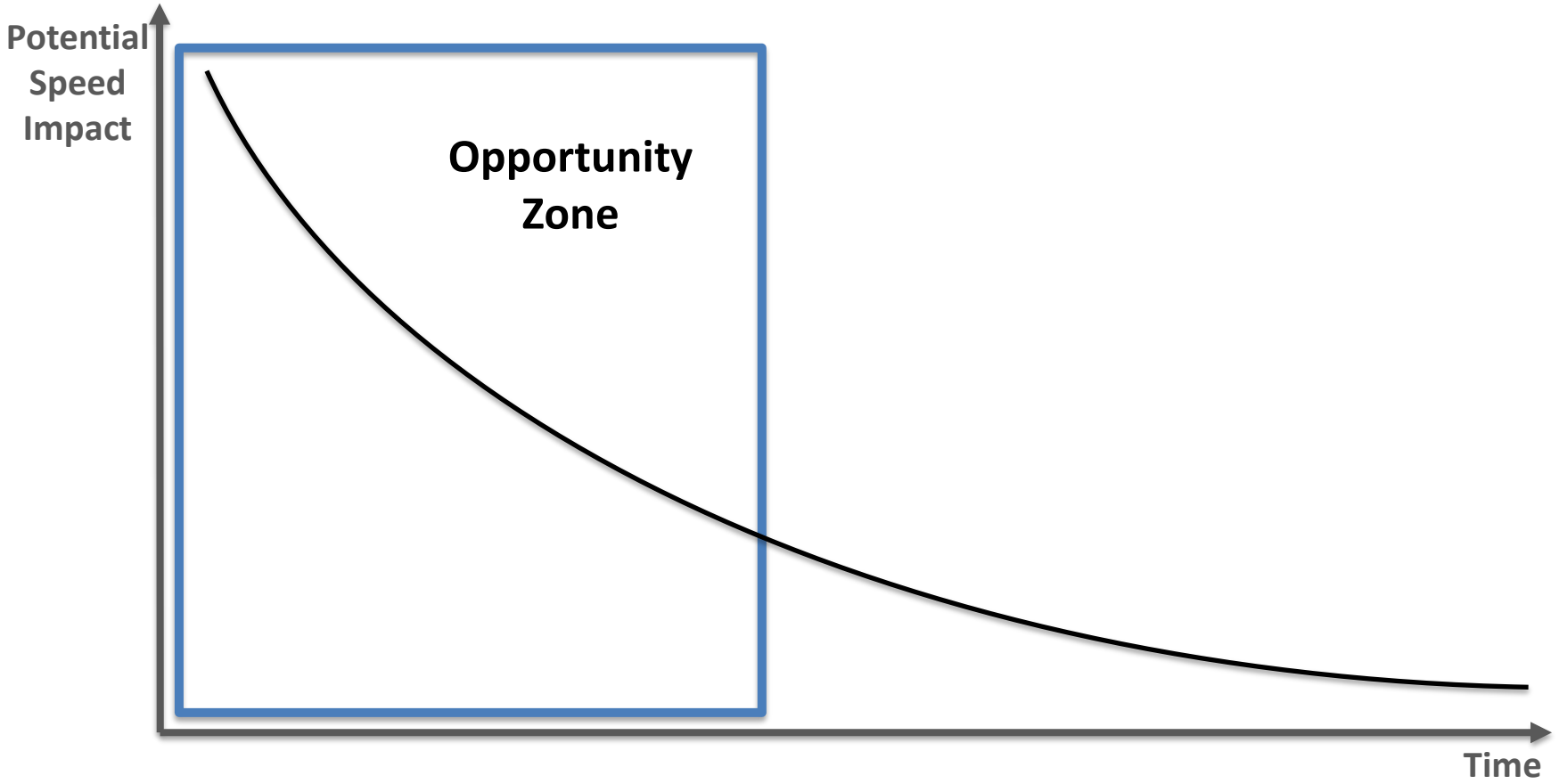

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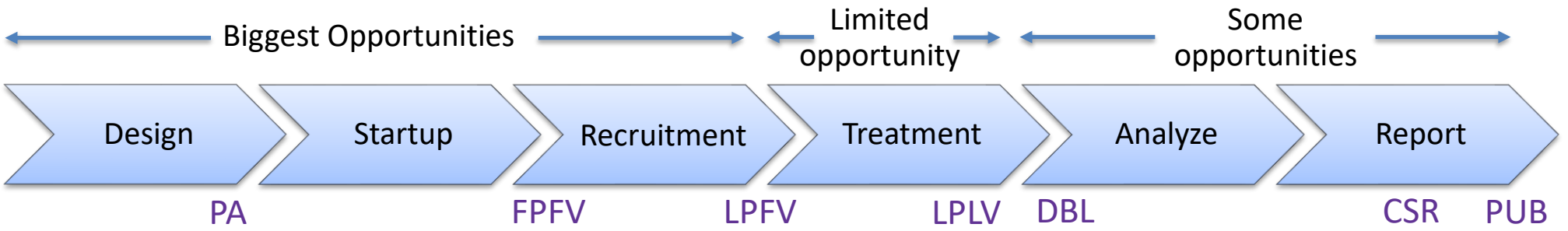
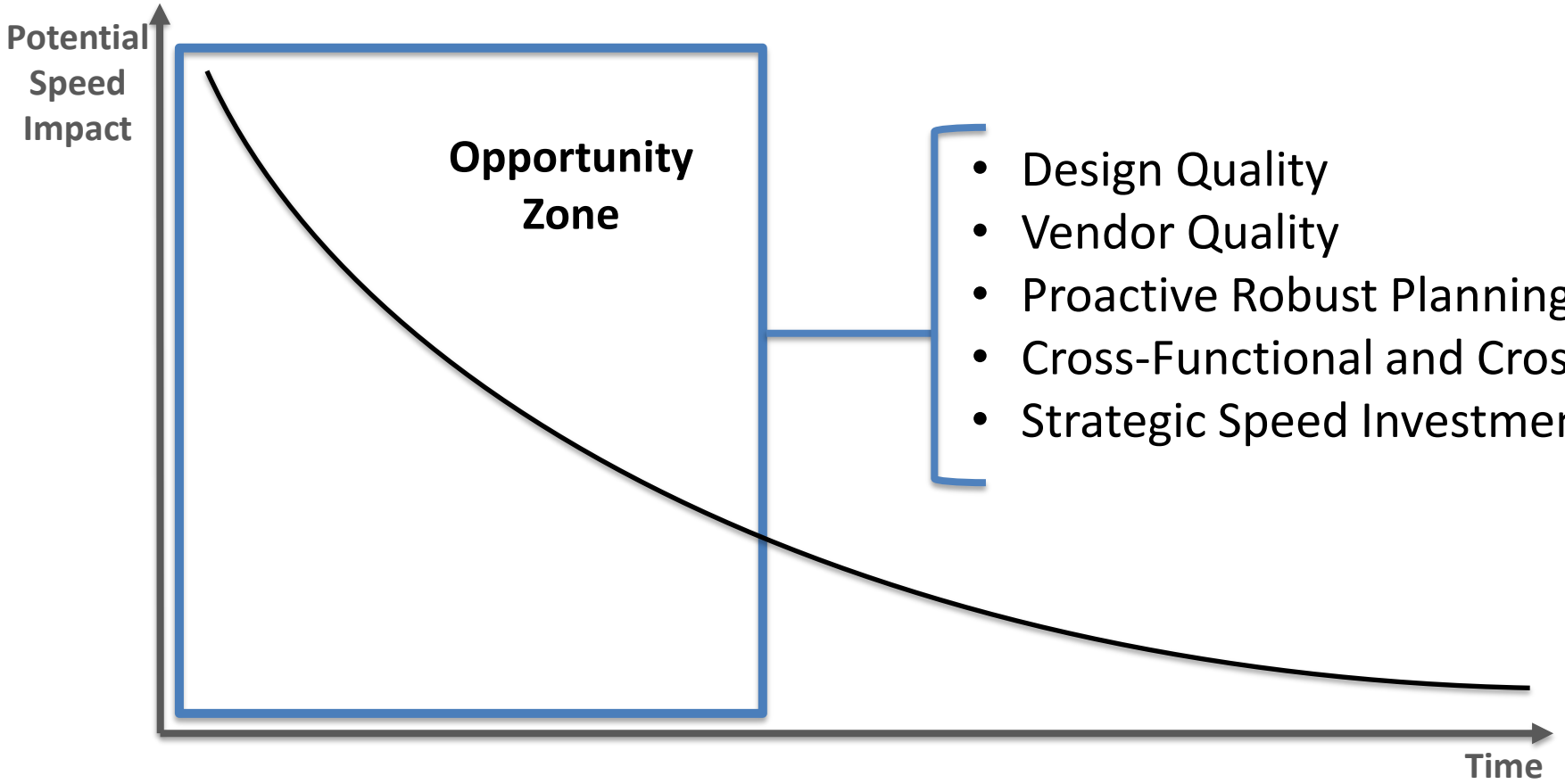
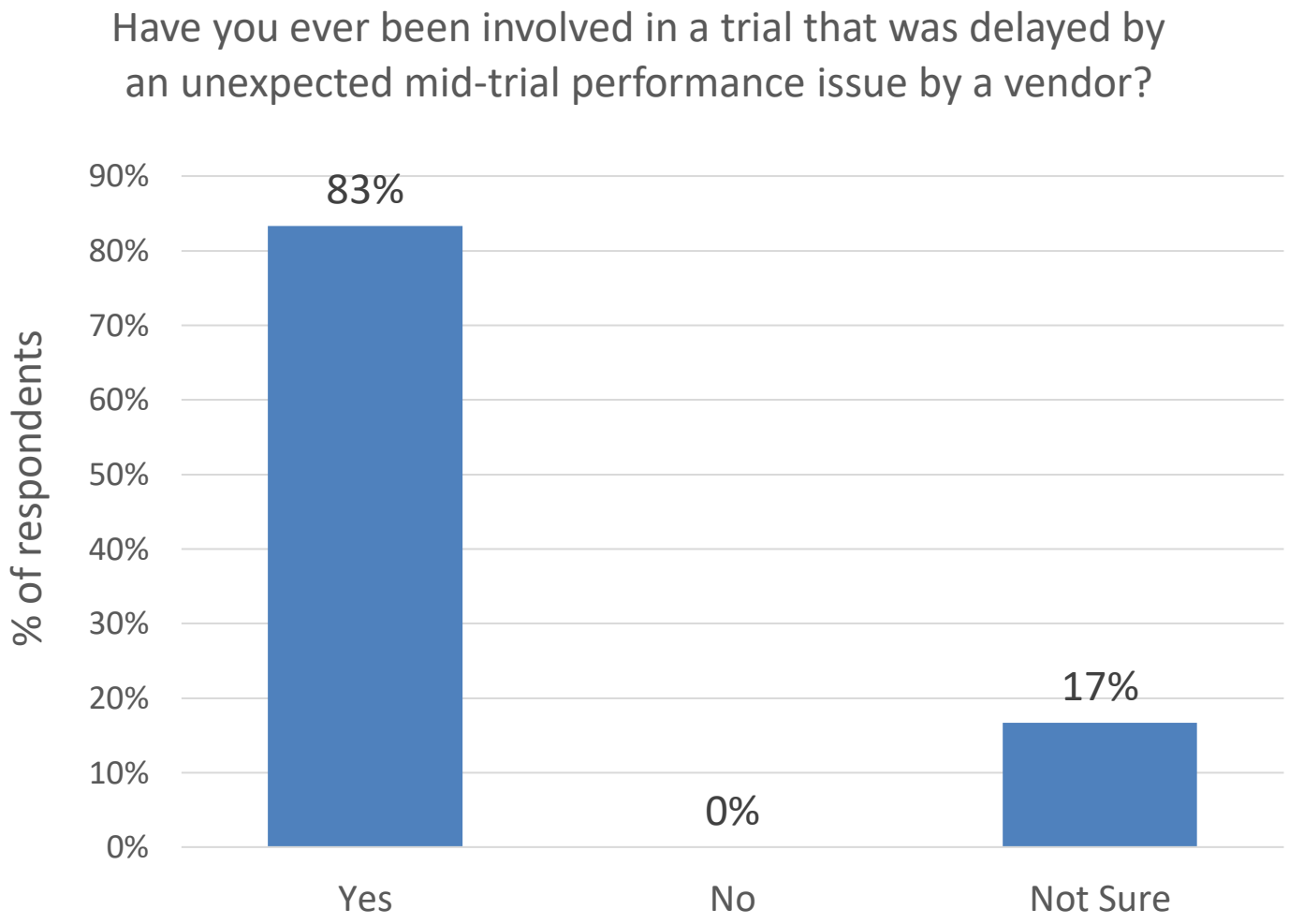




- Design Quality
- Vendor Quality
- Proactive Robust Planning and Risk Management
- Cross-Functional and Cross-Company Planning
- Strategic Speed Investments

Poll question



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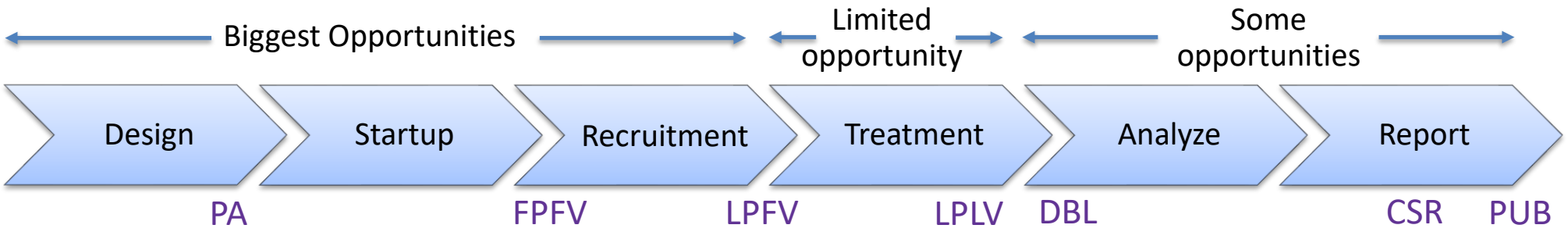
Work Smarter Not Harder to Accelerate Timelines



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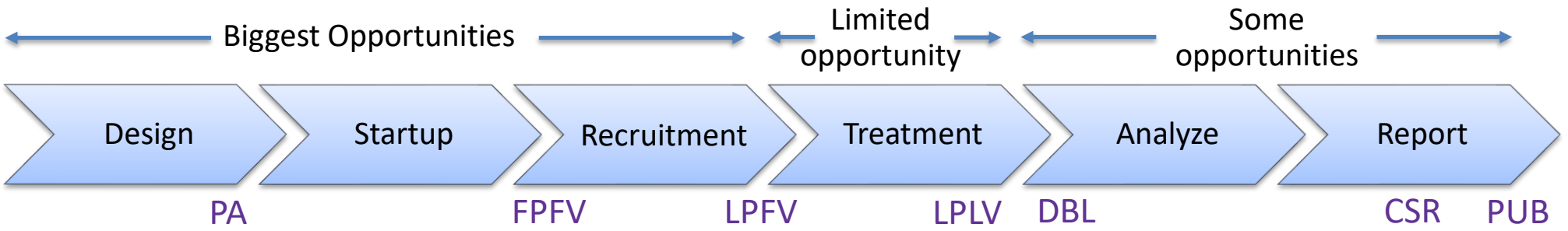
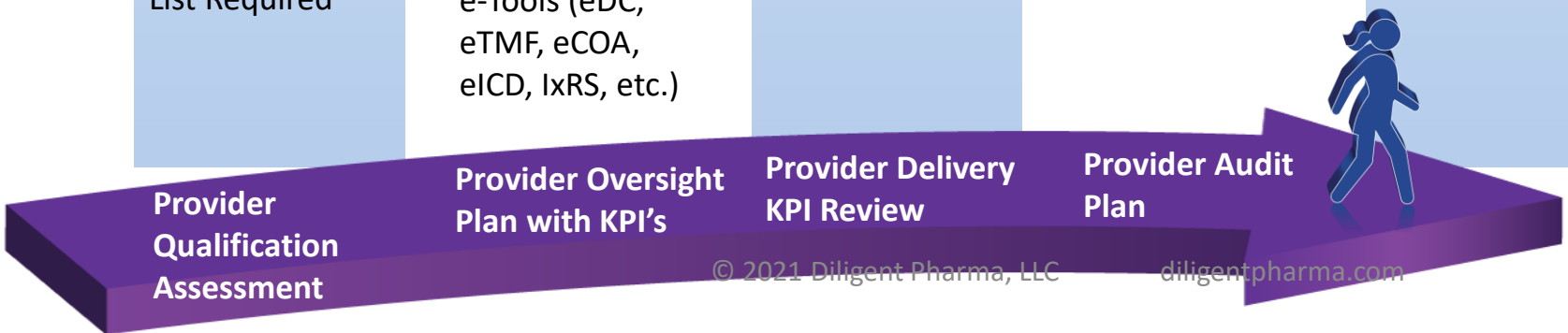


Design	Startup	Recruitment	Treatment	Analyze	Report
In-Silico Trial Modeling	Cross-Functional & Cross-Provider Proactive Planning	Recruitment Strategy & Plan	Proactive Data Management Plan	Finalize Data Cleaning	Interpret Data & Clinical Outcomes
Investigator & Patient Design Input	Risk Management Planning	Monitor & Adjust Plans	Develop SAP	Lock Database For Analysis	Write Clinical Study Report Conclusions
Quality By Design (QBD)	Multi-company Team with Clear Goals	Review Metrics, KPI's & QTL's	AI Signal Detection (Safety/EndPoint /Adaptive)	Planned & Ad Hoc Analysis	Write Public Disclosure Manuscripts for Publication
Clinical Trial Risk Assessment	Resource Plans & Contingencies				
Finalize Provider List Required	e-Tools (eDC, eTMF, eCOA, eICD, IxRS, etc.)				



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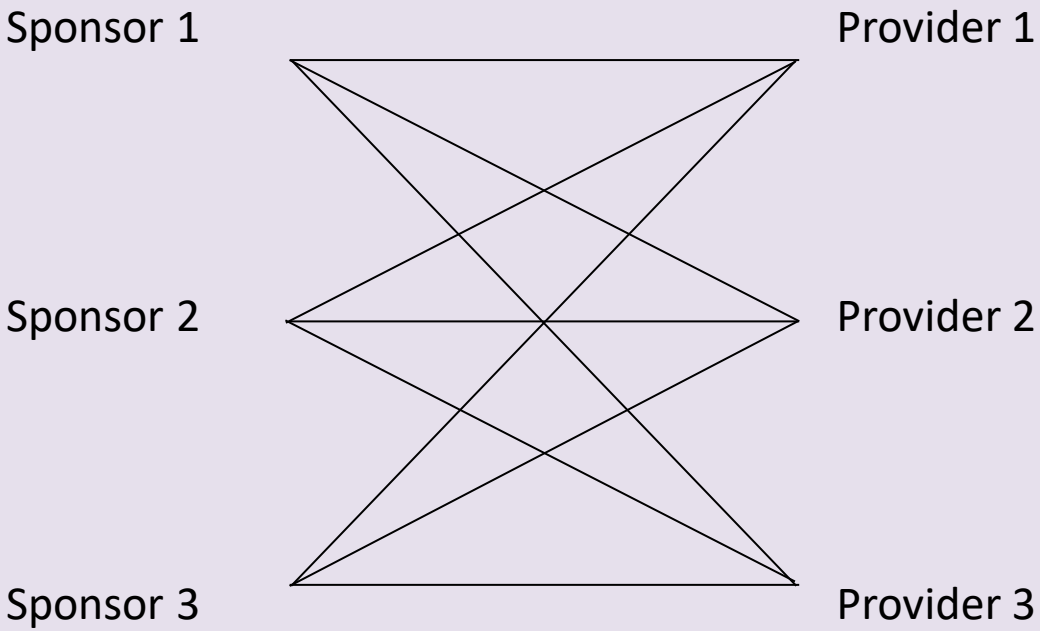
Sharing and leveraging supplier information with the Diligent Qualification Platform

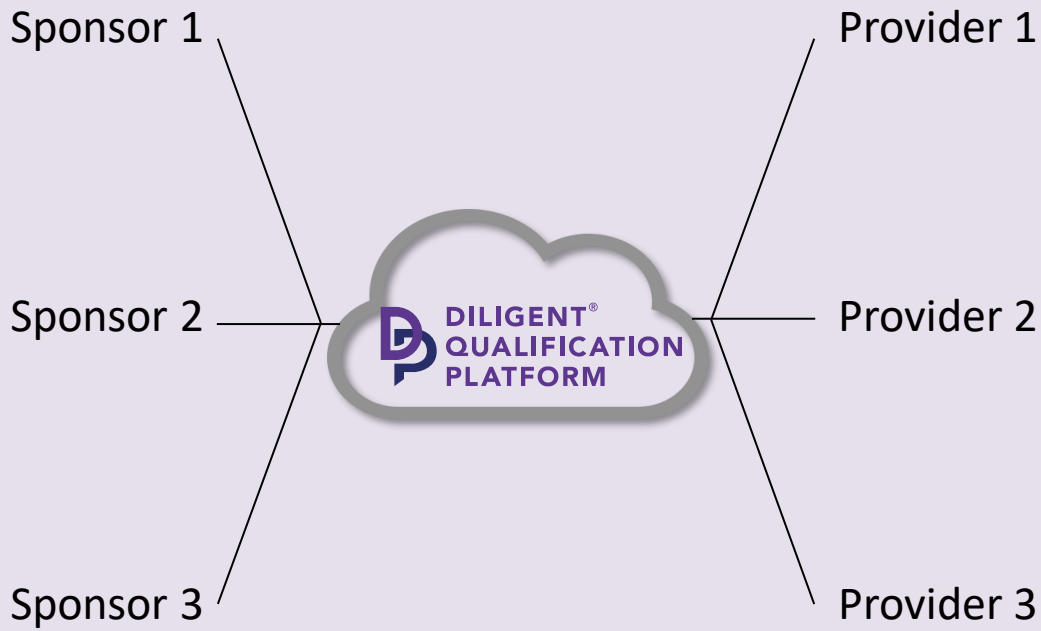
Current Qualification Process



~4,275
Pharma & Biotech
Sponsors

~4,900
Clinical & Technology
Providers

Diligent Qualification Process



Sources: EvaluatePharma; CenterWatch; William Blair & Wells Fargo Securities; TCSDD

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Benefits of shared vendor information

Standardization
Rigorous **Qualification Standards** and Shared Standards Information across your organization

Efficiency
Delivers a more **cost, time and resource efficient** model for sponsors and providers

Speed
Delivers **shorter timeframes** to onboard new providers and capabilities

Reduced Risk
Common Quality Standards mitigate risk and ensure compliance with regulations

Innovation
Drives innovation through enabling the use of qualified emerging technology providers

DILIGENT® QUALIFICATION PLATFORM

Diligent offers professional services supported by a web-based platform

Professional Services

- **Risk-based qualification procedures**
- **Standardization of RFI vendor questionnaire responses based on the latest regulations and standards**
- **Vendor Qualification Assessments (VQAs) and assessment strategy**
- **Multi-sponsor VQAs for time and cost savings**
- **Support for continuous provider oversight**

+

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Technology

Web-based access to a centralized service, with a robust database at its core, around which the features are built and delivered:

- **Completed RFI questionnaires and supporting information**
- **Searchable by key parameters**
- **Compare RFIs for multiple providers**
- **Request VQA Reports**
- **Shared VQA Calendar Function**

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Diligent/AQC Vendor Qualification Core Standards

Core standards for all clinical service providers

Organization

Financial Stability

Insurance Standards

Ethics/Anti-Bribery/ Anti Corruption

Quality management Systems

Third party Quality Management and Oversight

Document Management and Control

Risk-based Quality Management Systems

Privacy & Personal Data Protection

Computer Systems/ 21 CFR Part 11 Compliance

Operations and Project Management

Data Management and Transfer

Staffing and HR Management

Training

Facilities Management

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Diligent Vendor Qualification – Functional and Technical Capabilities

Clinical monitoring
Data management
Biostatistics
Medical writing
Phase I CRU

eHealth records
EDC
Electronic informed consent
Electronic Regulatory Binders (eISF)
Mobile HCP visits
Wearables/sensors
Telemedicine
eTMF
IRT, IxRS
COA, eCOA

Central laboratories
Medical imaging
ECG
IRT, IxRS
Biomarker laboratories
Bioanalytical laboratories
COA, eCOA

Patient recruitment & retention
Investigator contract budgets & payment
Investigational Product (IP) management
Pharmacovigilance
Mobile cardiac monitoring
Investigator site qualification

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Diligent Macro Processes

Sponsors

DILIGENT® QUALIFICATION PLATFORM

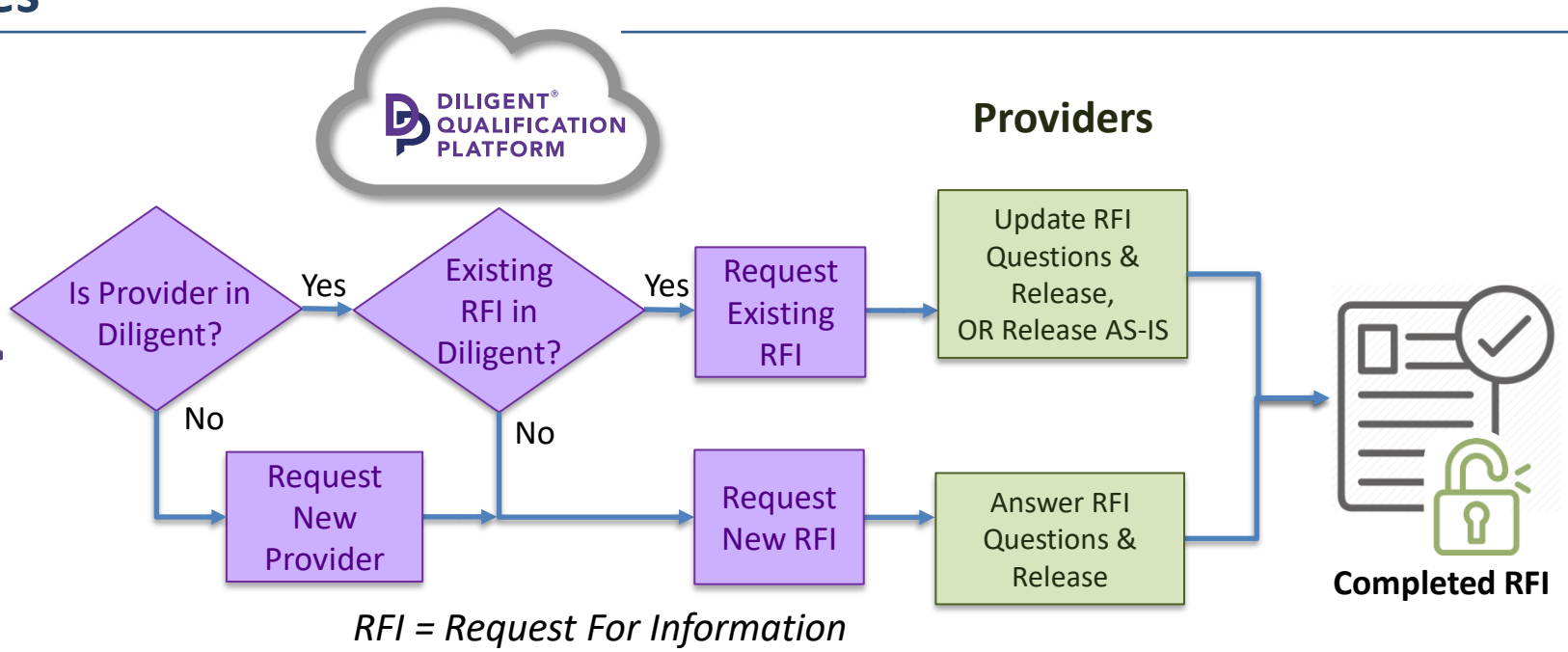
Providers

Sponsor needs to find additional clinical providers

Diligent Macro Processes

Sponsors

Sponsor needs to find additional clinical providers



RFI = Request For Information

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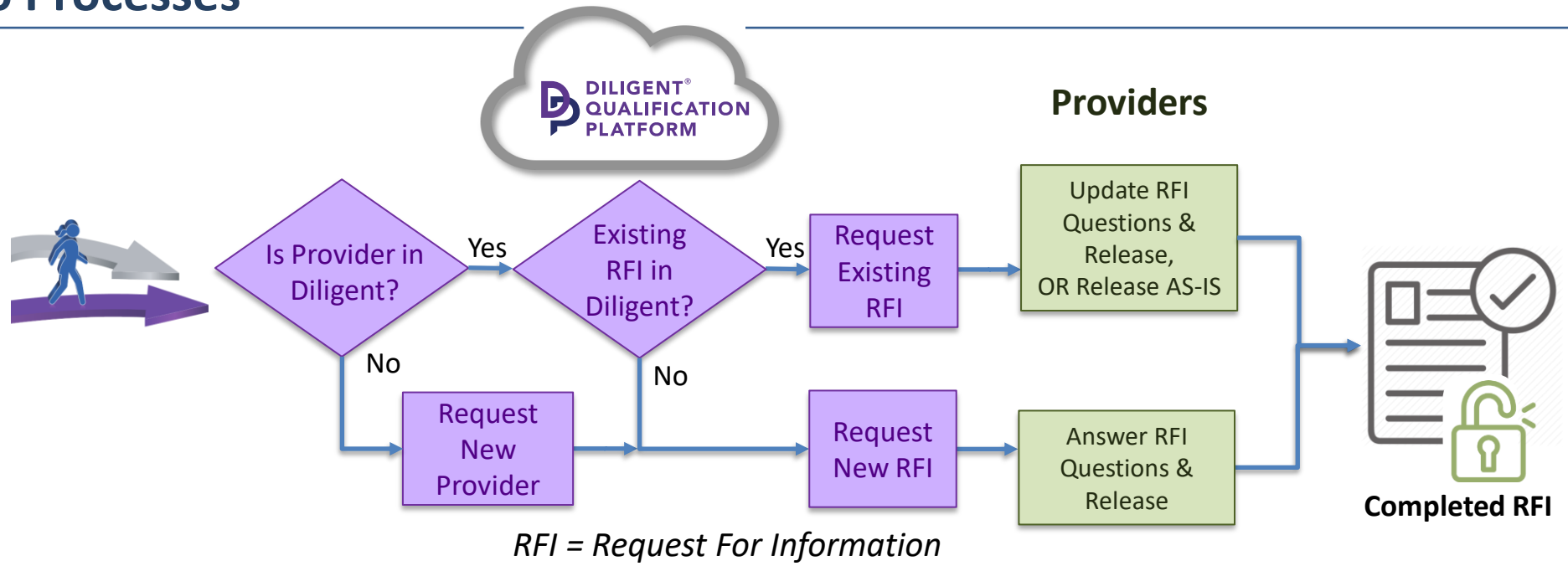
Diligent Macro Processes

Sponsor needs to find additional clinical providers

Sponsor needs to qualify Clinical Providers quickly



Diligent Macro Processes

Sponsors

DILIGENT® QUALIFICATION PLATFORM

Providers

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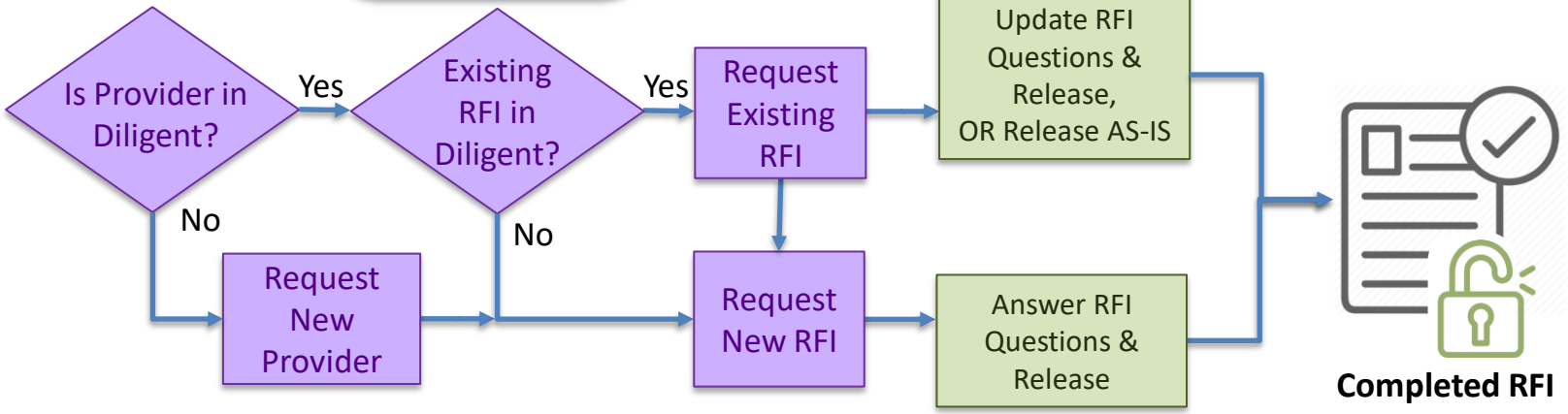
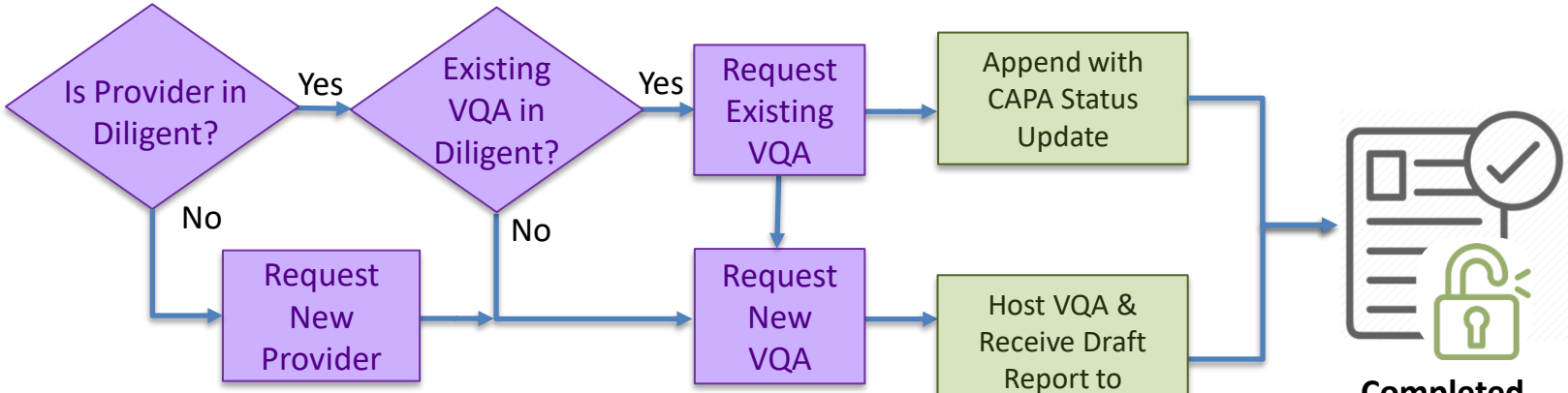


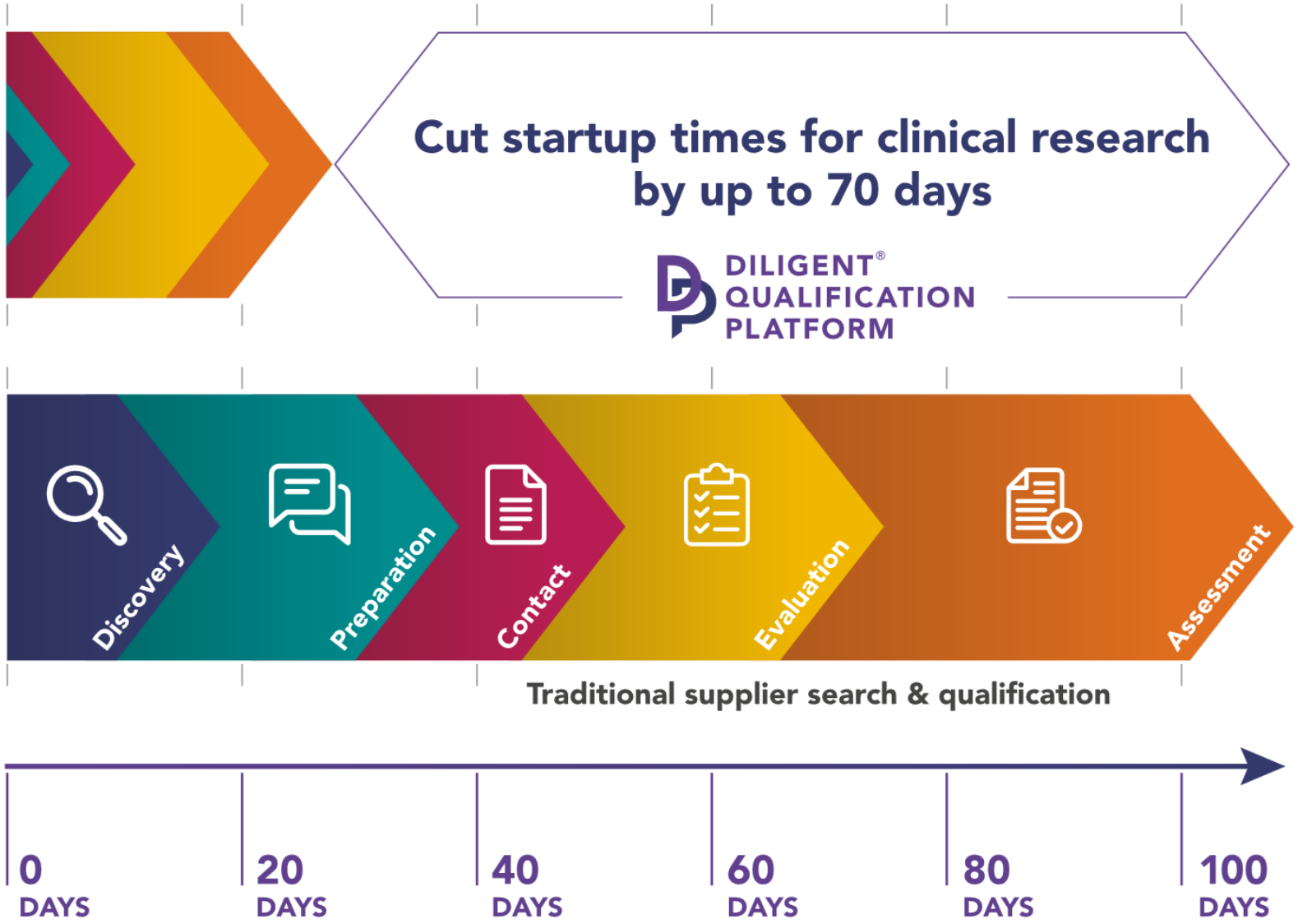
RFI = Request For Information

Sponsor needs to qualify Clinical Providers quickly



VQA = Vendor Qualification Assessment (Audit)

Diligent – Part of the Solution



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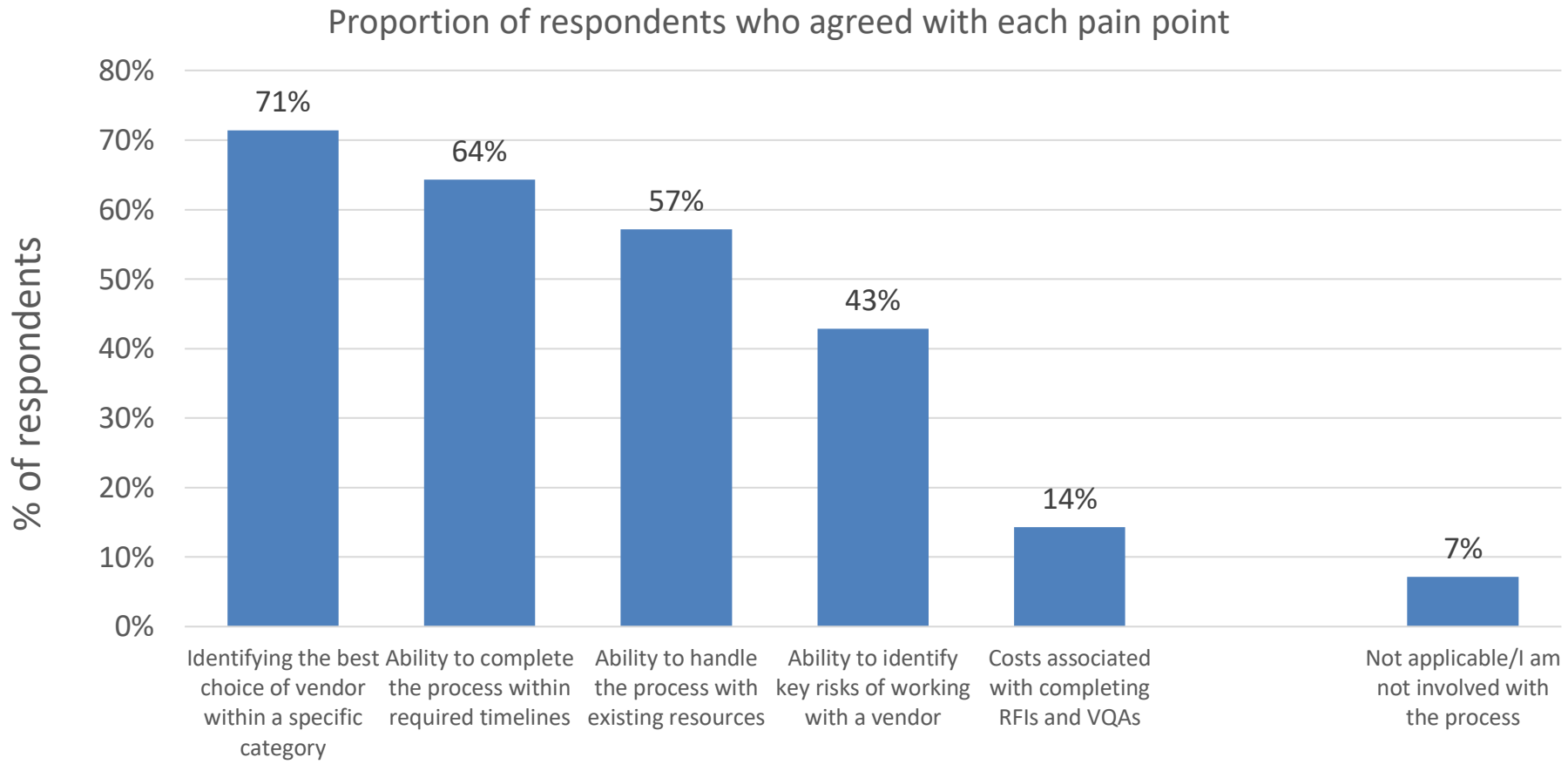
Poll question

What pain points are commonly associated with your organization's vendor qualification process? (Select as many as applicable)



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Helpful Links

Available Resources

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diligentpharma.com

Article:
Clinical Development Vendor Qualification
A “Check the Box” Exercise?
www.diligentpharma.com/article-clinical-development-vendor-qualification/

wcg™ AVOCA®

Virtual Meeting Recording:
Innovative Solutions to Provider Qualification Challenges
www.theavocagroup.com/news_events/virtual-meeting-innovative-solutions-to-provider-qualification-challenges/

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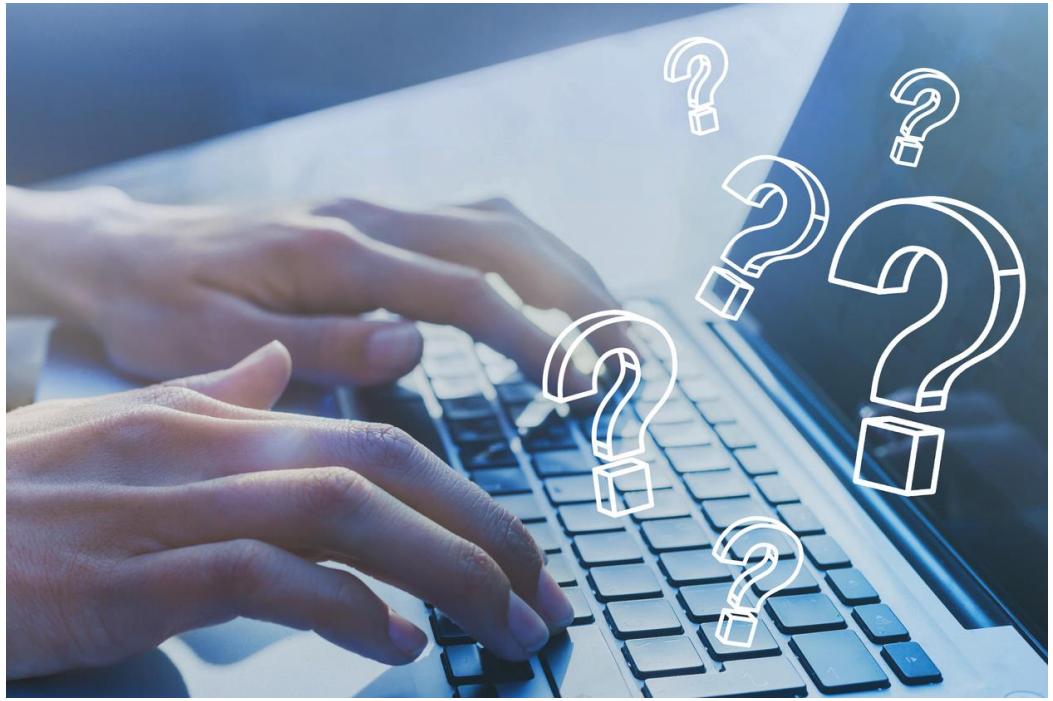

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