Empowering Sites for Clinical Trial Success Webinar Series – Part 1

Decoding the Top Site Challenges of 2024: The Complexity of Clinical Trials

Speaker Introductions

Sandy Smith, RN, MSN, AOCN,

SVP, Clinical Solutions & Strategic Partnering at WCG

Suzanne Rose, MS, PhD, CCRC, FACRP

Executive Director of Research at Stamford Hospital

Catherine Gregor

Chief Clinical Trial Officer at Florence Healthcare

Jenny Keppler

Vice President, Translational Medicine at Translational Drug Development (TD2)

Today's Agenda

1. 2024 Site Challenges Report Overview
2. Data & Insights on the Complexity of Clinical Trials
3. The State of Site Tech Adoption
4. Assessing Staff Workload
5. A New Era of Complex Trial Designs
6. Panel Discussion & Audience Questions
7. Conclusion

Polling Question #1:

What type of organization do you represent?

2024 Clinical Research Site Challenges Report Overview

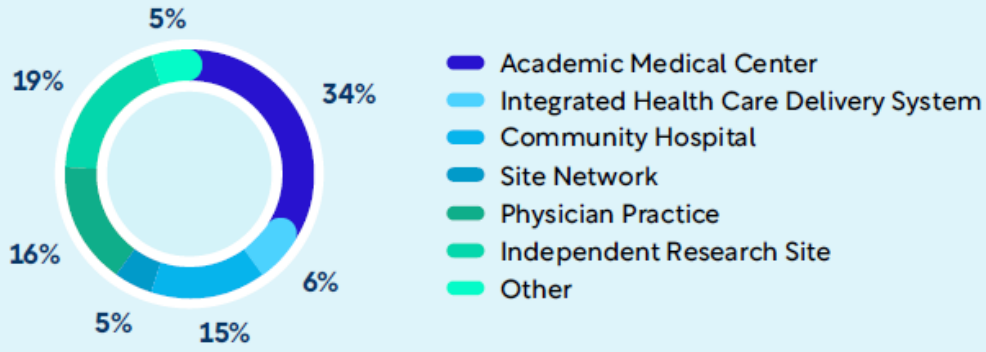
- WCG surveyed over 850 clinical research sites between April and June of 2024 to gain insights surrounding the top challenges they are facing, solutions they are implementing, and more.
- Utilizing the survey results, industry data, and insights from WCG experts, we published our 2024 Clinical Research Site Challenges Report in October.
- In addition to the survey results, this report also features actionable recommendations for sites, sponsors, and CROs to overcome barriers and enhance clinical trial efficiency.

The full report can be downloaded for free at: www.wcgclinical.com/challenges

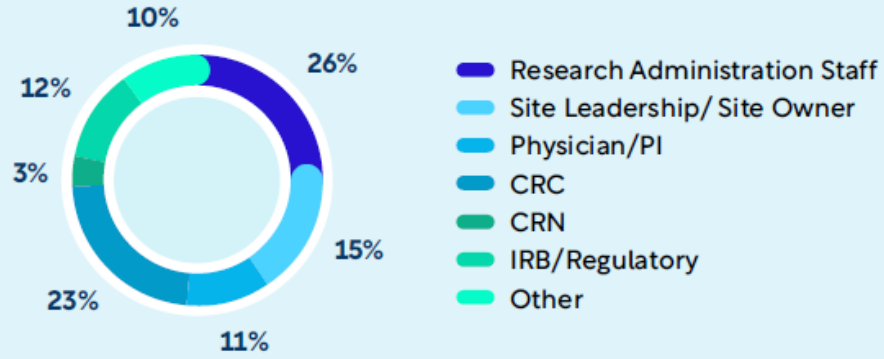
2024 Clinical Research Site Challenges Report - Background

Site Types, Job Titles, and Site Region

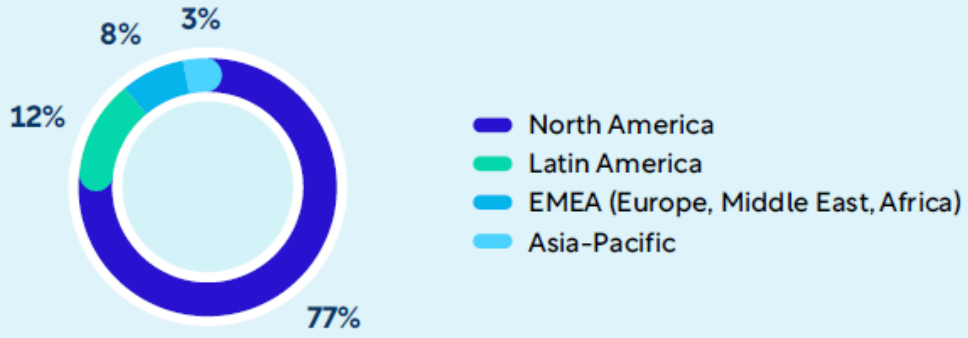
What type of research site do you represent?



What is your role at your research site?

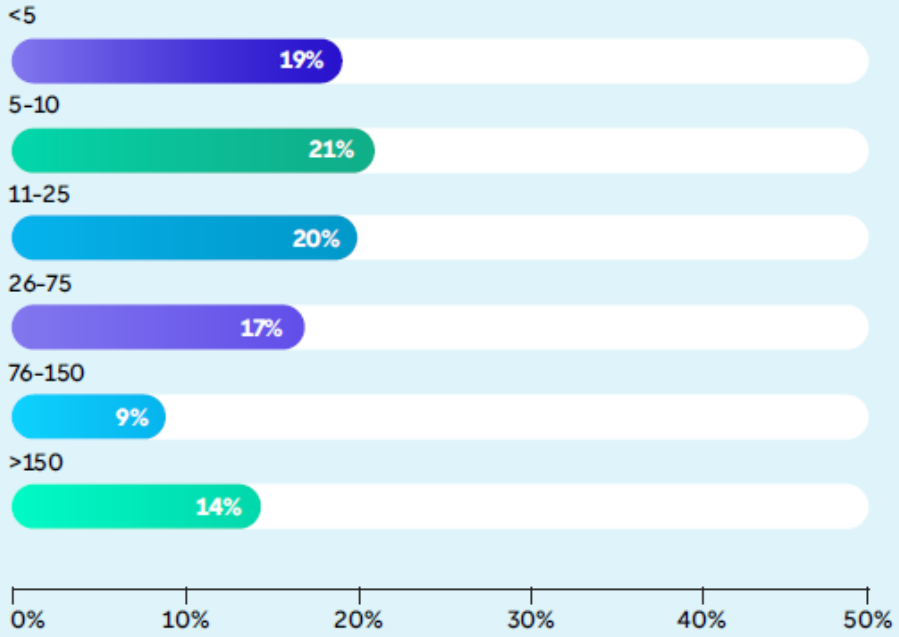


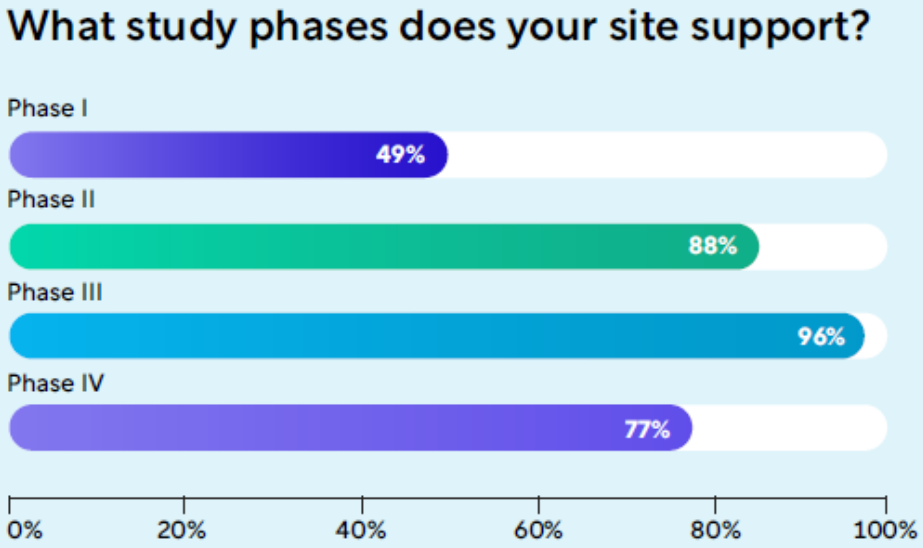
What region is your site based in?



2024 Clinical Research Site Challenges Report - Background

Study Phases and Number of Enrolling Trials



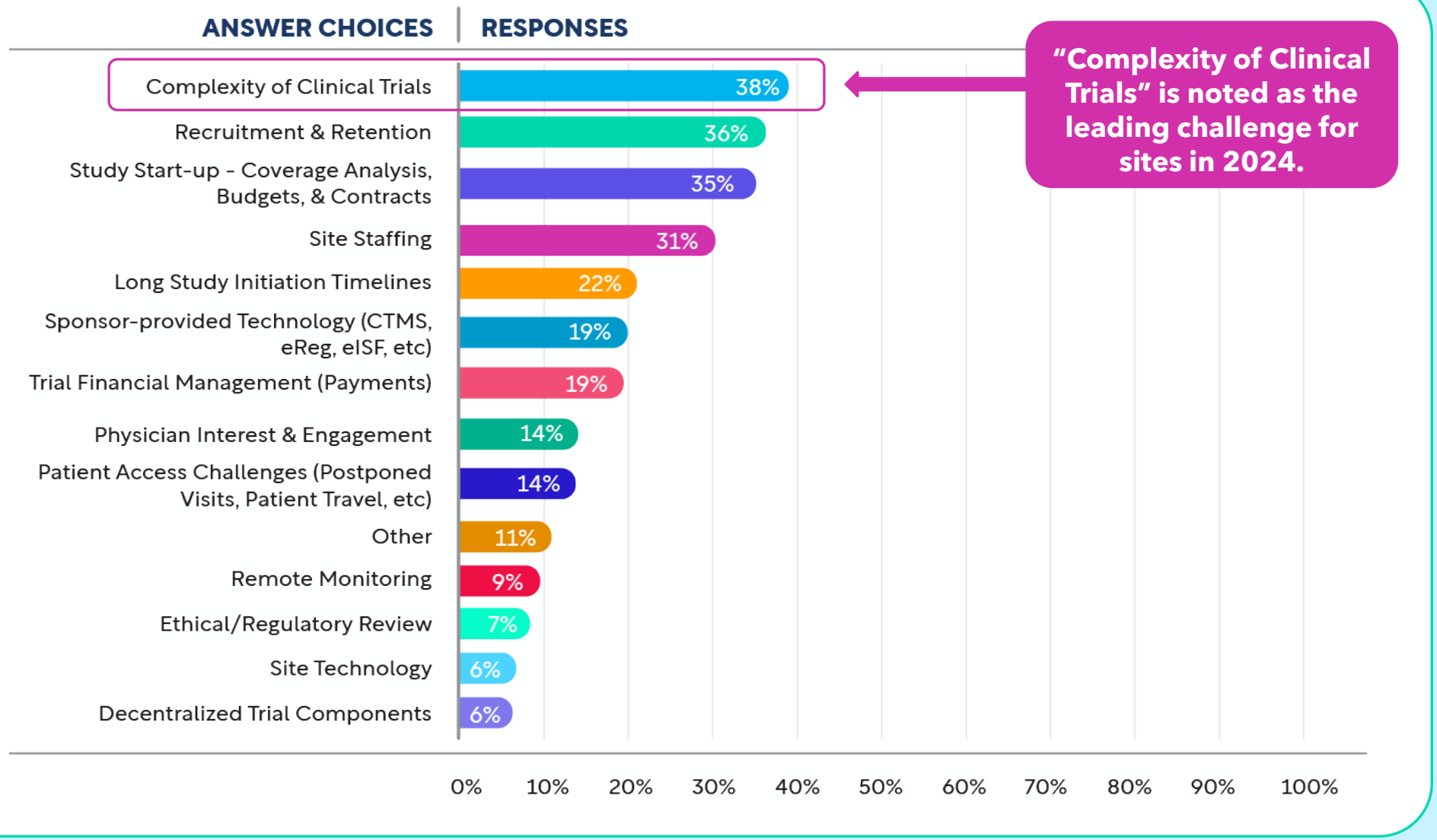


Polling Question #2:

What are the top factors you believe are contributing to clinical trial complexity?

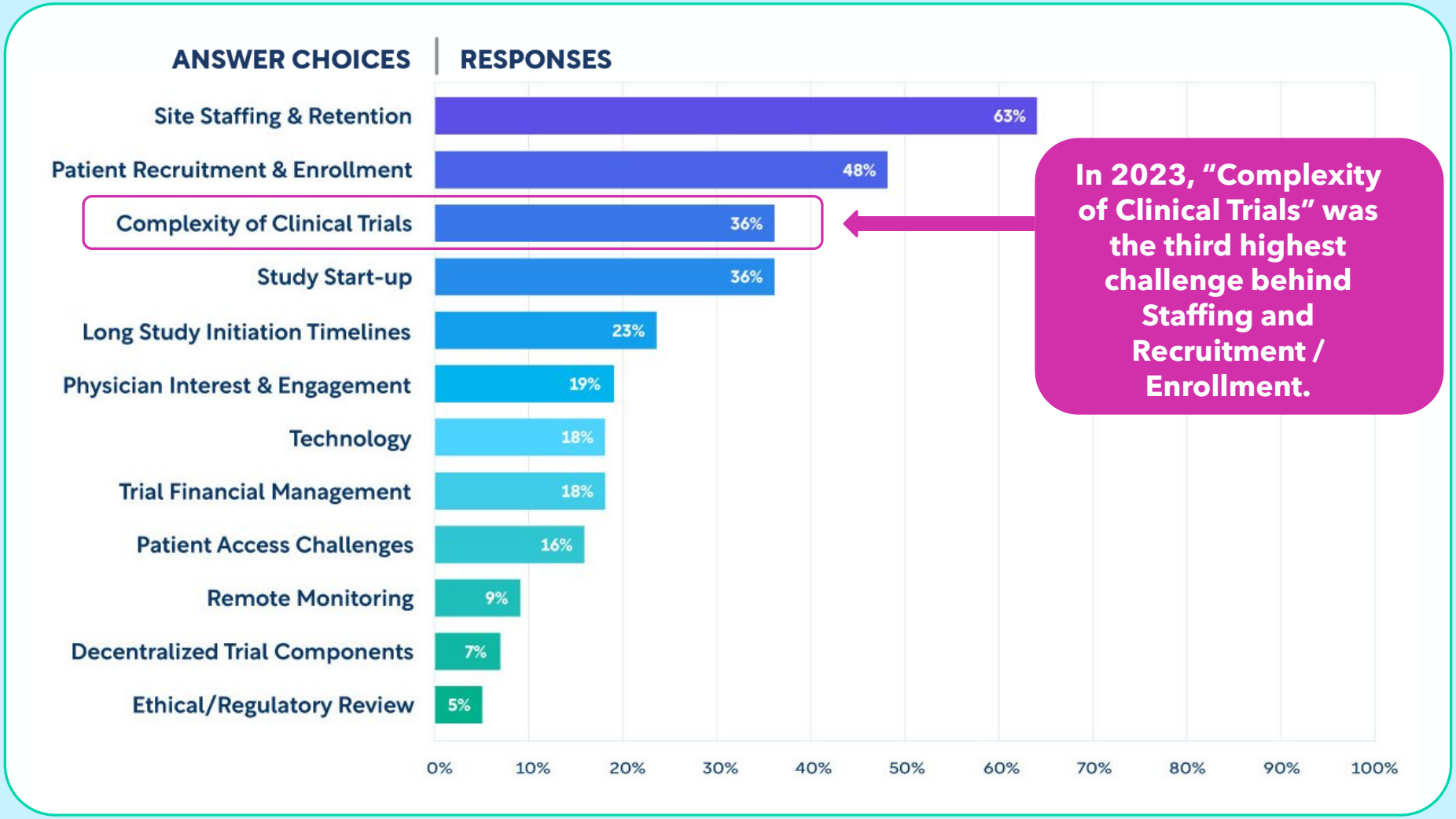
The Top Research Site Challenges in 2024

According to WCG's 2024 Clinical Research Site Challenges Survey



The Top Research Site Challenges in 2023

According to WCG's 2023 Clinical Research Site Challenges Survey



Examining the Increasing Complexity of Clinical Trials

Clinical Trial Durations by Phase

Phase I Trials

Time Period	Mean Trial Duration in Months
2008-2013	13.8
2014-2018	14.8
2018-2021	20.3

Phase II Trials

Time Period	Mean Trial Duration in Months
2008-2013	27.1
2014-2018	30.2
2018-2021	40.6

Phase III Trials

Time Period	Mean Trial Duration in Months
2008-2013	26.8
2014-2018	28.5
2018-2021	39.4

Source: Tufts CSDD

Examining the Increasing Complexity of Clinical Trials

Trends in Substantial Protocol Amendments

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

Source: Tufts CSDD

Examining the Increasing Complexity of Clinical Trials

Why Sites are Feeling the Burden – Protocol Complexity, Endpoints, Data

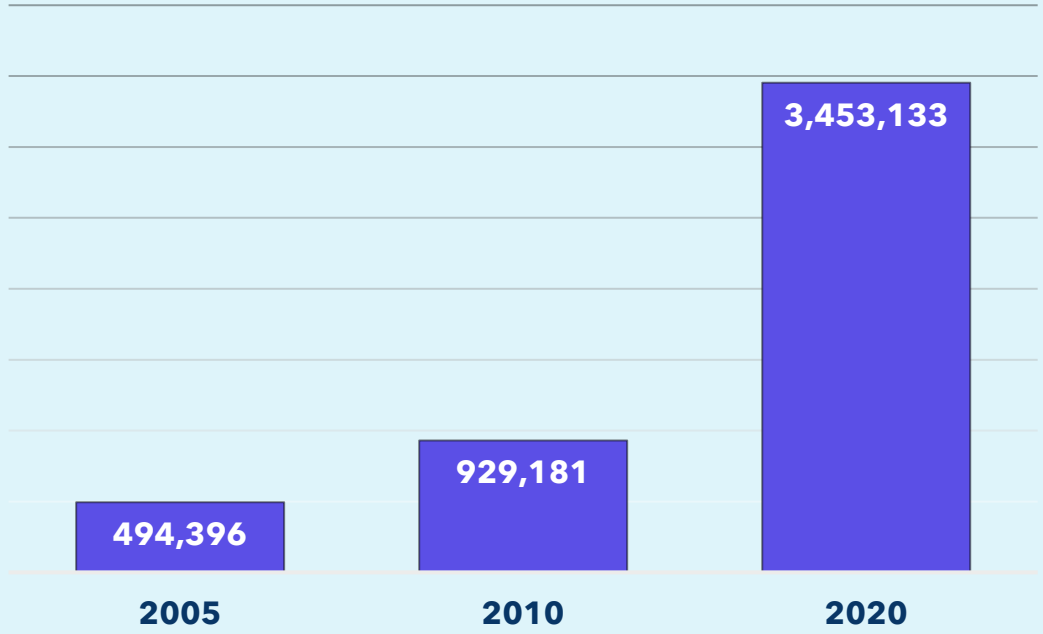
42% increase in procedures required in phase III trials since 2015.

37% increase in number of endpoints in phase III trials since 2015.

47% of sites cite "simplifying protocol complexity" as a top area for sponsors to address when it comes to their site's operating viability.

46% of sites say "soliciting site input on study design and implementation is a top area for sponsors to address."

Average Number of Data Points per Pivotal Trial



Source: Tufts CSDD

Examining the Increasing Complexity of Clinical Trials

Why Sites are Feeling the Burden - Technology

42% of sites stress the need for sponsor acceptance of their technology in study participation, according to Florence's 2024 State of Technology Enabled Clinical Trials report.

43% of sponsors view their software's adoption as a key selection criterion according to Florence's 2024 State of Technology Enabled Clinical Trials report.

38% of sites find sponsor-provided technology inadequate, according to Florence's 2024 State of Technology Enabled Clinical Trials report.

60% of research sites are using more than 20 systems daily, according to a 2022 poll conducted by SCRS.

Source: Florence Healthcare and Society for Clinical Research Sites

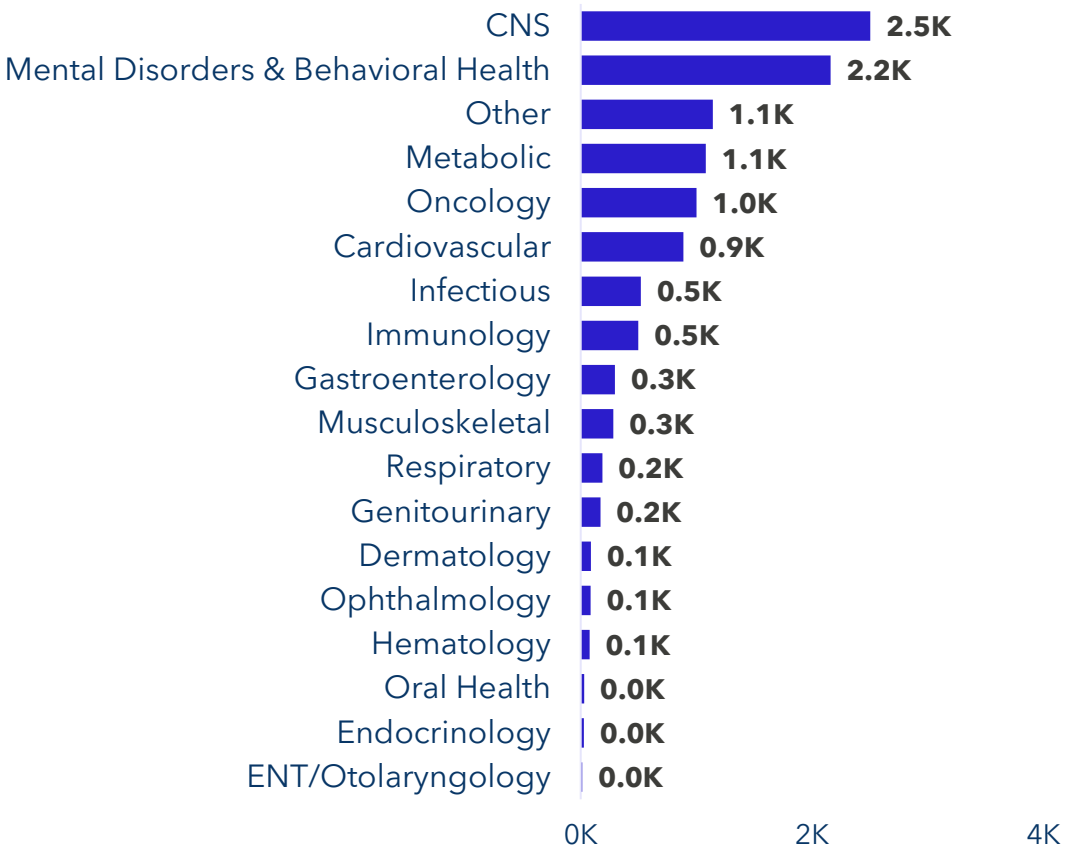
25% **of independent sites, site networks, and physician practices** ranked sponsor-provided technologies as a top challenge.

16% **of AMCs, community hospitals, and health systems** ranked sponsor-provided technologies as a top challenge.

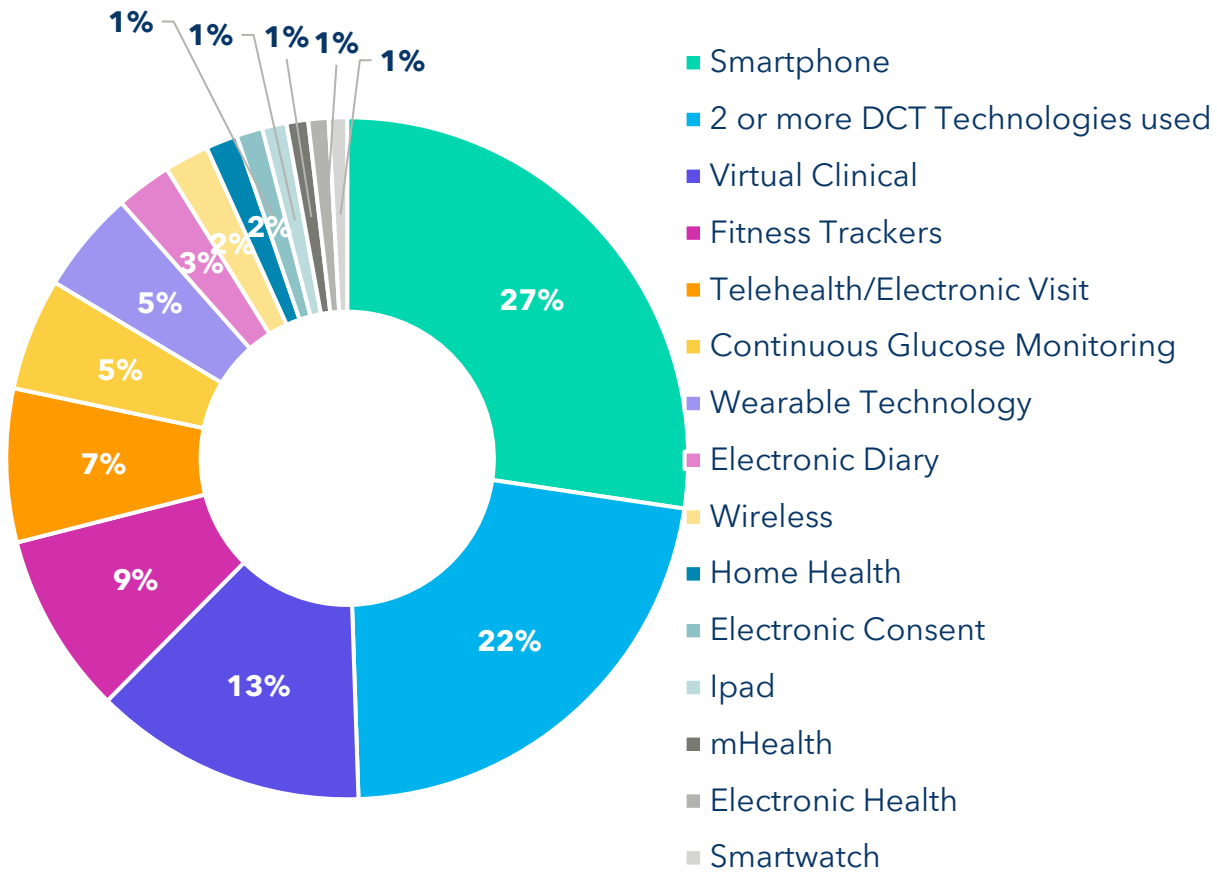
Source: WCG's 2024 Clinical Research Site Challenges Report

Smartphones & Two or More DCT Technologies Have the Highest Utilization When Conducting DCTs

TA's Utilizing DCT Components Most Frequently



Top 15 Technology Types Utilized in DCTs



Source: WCG ClinSphere™

State of Site Tech Adoption

Catherine Gregor
Chief Clinical Trial Officer

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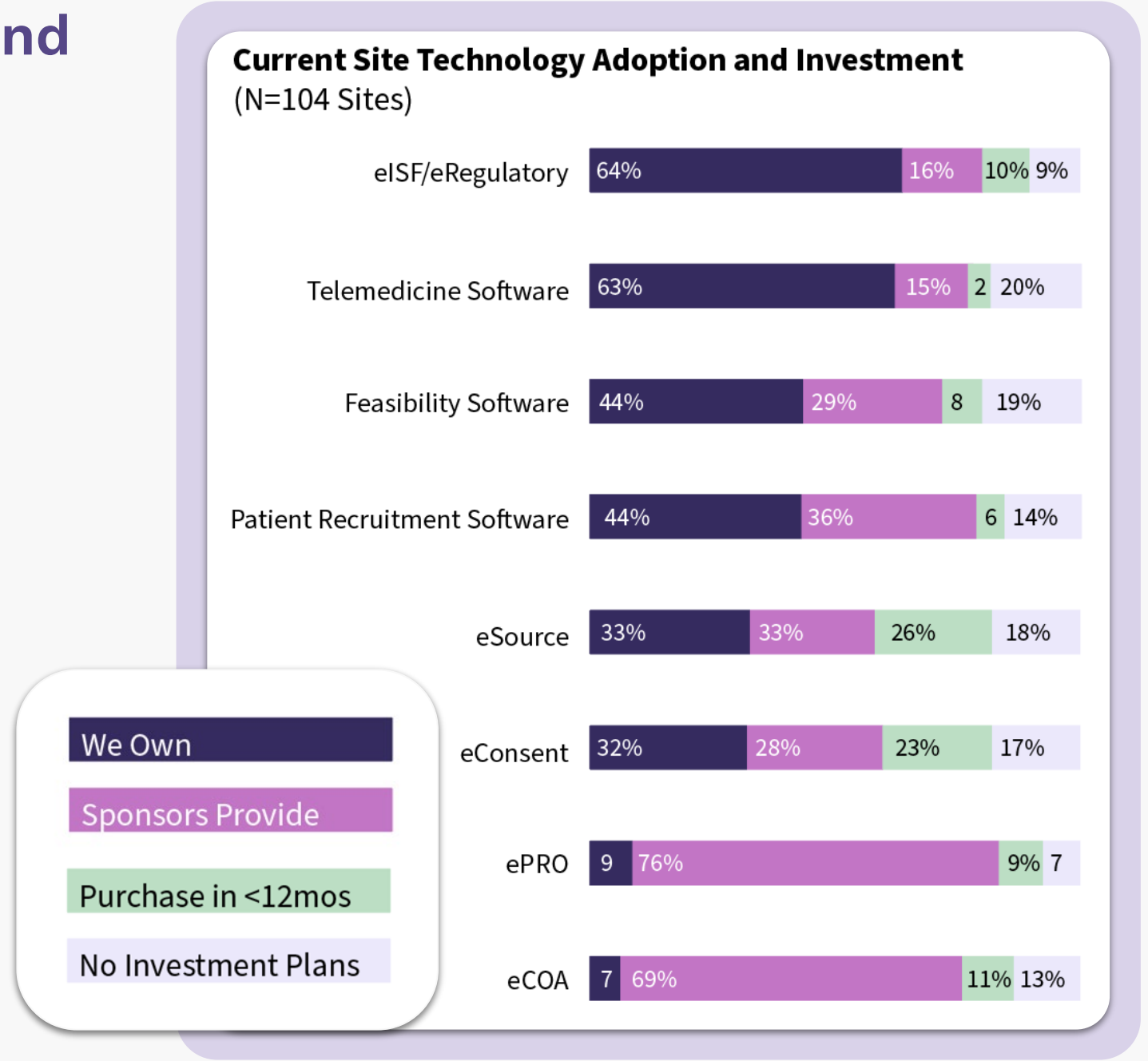
2024 Site Tech Adoption and Investment Data

- **Preferences in the tech sites own themselves clearly beginning to show.**
- **eCOA and ePRO remain almost entirely sponsor deployed.**
- **Tech gap emerging between AMC/Large Systems and independent sites sponsors must collaborate with sites to solve.**



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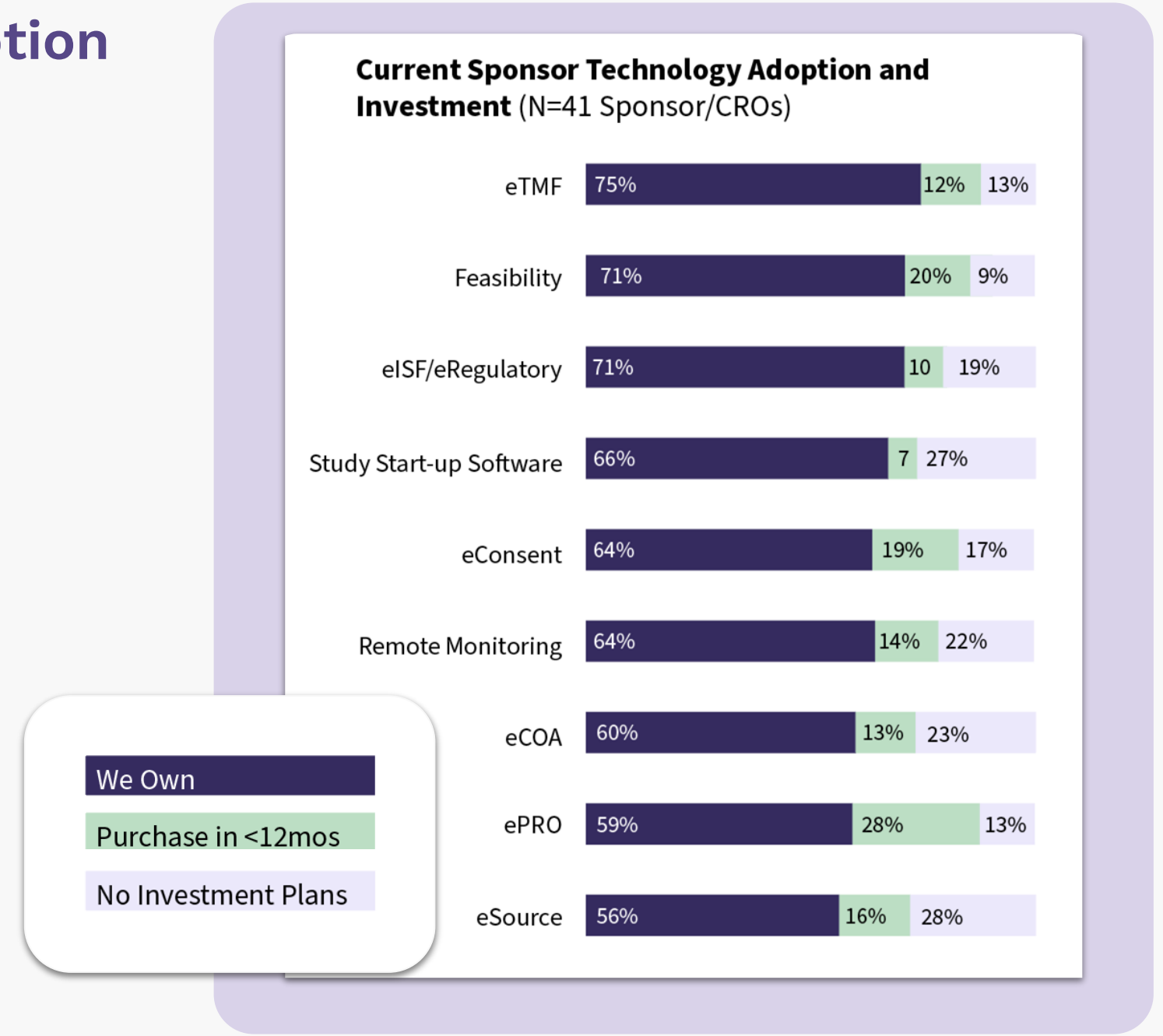
2024 Sponsor Tech Adoption and Investment Data

Sponsors now investing in site-based technology almost across the board.

Clearer definitions needed of what counts as certain software types “Start-up”, “Feasibility” and “Monitoring” most impacted.



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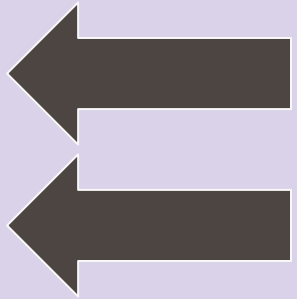
Barriers to Investing in Technology

	Sites Agree N=141	Sponsors Agree N=41
Budget and cost concerns	68%	63%
Integrations	60%	57%
Transition to Tech	44%	41%
IT/Data/Security	41%	25%
Site Team Adoption	25%	41%
Compliance	24%	18%



2024 Florence State of Industry Report

Key Tech Considerations in Other Party

Sites Ranking as #1 or #2
N=141

65%	Is accepting of site-owned technology solutions
54%	Conducts remote monitoring activities
30%	Provides technology for remote document exchange
28%	CRAs/Monitors trained to use monitoring software

Sponsors Ranking as #1 or #2
N=41

56%	Is accepting of sponsor-deployed tech
56%	Provides technology for remote document exchange
49%	Uses technology that supports remote monitoring
21%	Supports remote Source Data Review + Verification

2024 Florence State of Industry Report

Key Changes in 2023 Impacting 2024—The First Step is Giving a Damn

82.76%

of sponsors say their organization cares more about the sites technology experience than they did 1 year ago.

55%

decrease in Email usage for document exchange between Sites and Sponsors from 2020 to 2024.

95.25%

of sponsors believe sites value their software, yet only 62.5% of sites feel that sponsors address their tech needs.

Impact of Tech On Study Operations

STARTUP

- **Automate startup tasks power essential document exchange** reducing timelines and streamlining communication…resulting in a 40% time-savings

MONITORING

- **Enable remote monitoring** to shift work from CRAs onsite to centralized resources
- **Improve inspection readiness** at sites to improve eTMF acceptance rate from 65% to 90%
- **Increase real time access by removing travel barriers** and increasing frequency of data monitoring

Economic Impact of Site Tech for Sponsors

- Save **4 weeks on average at startup**
- Save **2 weeks at closeout**
- Save **travel costs**
- **Reduce cash burn** by up to $1M per study

Assessing Staff Workload

Suzanne J. Rose, MS, PhD, CCRC, FARCRP

Executive Director of Research, Stamford Health

Background

- Many challenges associated with managing clinical trials
- Today's trials are heterogeneous and increasing in complexity while the funding is less
  - ✓ Need to work efficiently and effectively
  - ✓ Turnover and burnout is high
  - ✓ Data management quality negatively affected
- How many patients or studies can one research coordinator handle?

*"….institutions increasingly realize they need a convenient, comprehensive, versatile, logical, sensible, equitable, and objective tool for measuring Clinical Research Coordinator (CRC), workload…"**

*Gwede C K, Johnson D, & Trotti A: Measuring the workload of clinical research coordinators, part 1: Tools to study workload issues. Applied Clinical Trials: 40-44, January 2000

Good, M. Assessing Clinical Trial-Associated Workload. 2014 AICRN Annual Conference, November 6, 2014.

Tool Integration

Clinical Research Workload Tool (CRWT) scoring model

- Based on core tasks that are routinely completed within any clinical trial, regardless of complexity. These include (but are not limited to):
  - Protocol review, informed consent form review, IRB submission, source documentation completion, adverse event monitoring, safety reporting, patient visits, ongoing protocol administration (amendment submission, e.g.), and query completion.

The CRWT score (protocol workload) is:

- Determined by the type of intervention and # of incremental procedures included.
- Described as the work required to maintain a study regardless of patient involvement.

Tool Integration – DRUG Studies

The following scores are utilized in CRWT scoring of the protocol (1-8, 1 being the lowest and 8 being the greatest, i.e. most complex)

1. Non-treatment trial; Single-contact events include quality of life, survey, blood samples, etc.
2. Non-treatment trial; Multiple-contact events include quality of life, survey, blood samples, etc.
3. Phase II/III/IV Investigational, non-drug; Imaging, and/or exercise studies.
4. Treatment trial, phase II, III, or IV. This includes any one Research Staff Procedure (RSP)* **and/ or** one non-Research Staff Procedure (nRSP)** with one occurrence.
5. Treatment trial, phase II, III, or IV. This includes multiple RSP **or** multiple nRSP.
6. Treatment trial, phase II, III, or IV. This includes any multiple RSP + single nRSP or multiple nRSP + single RSP.
7. Treatment trial, phase II, III, or IV. This includes any multiple RSP + multiple nRSP.
8. Any phase I trial.

Tool Integration – DEVICE Studies

The following scores are utilized in CRWT scoring of the protocol (1-8, 1 being the lowest and 8 being the greatest, i.e. most complex)

1. Post-market device trial; Single-contact events include quality of life, survey, blood samples, etc.
2. Post-market device trial; Multiple-contact events include quality of life, survey, blood samples, etc.
3. Imaging, and/or exercise studies.
4. Pre-market device trial. This includes any one Research Staff Procedure (RSP)* **and/ or** one non-Research Staff Procedure (nRSP)** with one occurrence.
5. Pre-market device trial. This includes multiple RSP **or** multiple nRSP.
6. Pre-market device trial. This includes any multiple RSP + single nRSP or multiple nRSP + single RSP.
7. Pre-market device trial. This includes any multiple RSP + multiple nRSP.
8. Pre-market device trial with required in-patient stay or overnight requirement.

Tool Integration

Added weights to the CRWT score (protocol workload) include:

- Monitoring (frequency < 3 months or 100% source document verification) (+0.5)
- Industry sponsor/CRO factor (+0.5)
- Duration of treatment or number follow-up visits (+0.5)
- Multiple surveys/questionnaires (+0.5)
- Protocol Mandated In-Patient (+0.5)
- Mentoring New Staff or following subjects at satellite (+.15)

Other factors affecting the CRWT score:

- Utilization of a RA, RC, DM reduces the scale by .25 (25%) of the original CRWT score

Example Study Synopsis and Protocol Scoring Using the CRWT

I/E	Arms	Study Design	Screening	Visits	ICF
9 Inc 13 Exc	3	Visits every 2 weeks; all require fasting labs	2-week placebo run-in	All require full physical exam, labs, and questionnaires	PGx sub-study at all sites
Test Article	**Study Duration**	**TA and/or Disease**	**Procedures**	**Safety**	**Source Docs, Diary, QOL**
Oral drug	6 months treatment period + 2 week follow-up	Early onset Type 2 Diabetes	No glucose tolerance testing' standard clinical evaluations	Expedited reporting for protocol defined glycemic events	Source not provided; electronic diary for glycemic events; paper questionnaire

How do we calculate?

- Protocol Score
  Treatment trial, phase II, III, or IV. This includes any multiple RSP + multiple nRSP (scored a 7)

- Added Weights
  Duration of treatment or number follow-up visits (+0.5)
  Multiple surveys/questionnaires (+0.5)

CRWT score of 8

Total Workload Calculation

- Determine **protocol workload**
- Multiplying the CRWT score by the number of patients in the study as well as the weight designated for study status gives the **case workload**.
- Adding the protocol workload plus the case workload will give the **total workload**.

CRWT scoring sheet – Rheumatology Study

Step 1:		
score protocol 1-8 based on definition	8	
add weights based on list	0	
deduct weights based on list	0	no RA assigned to study
Protocol Workload score	8	
Step 2:		
Determine number of enrolled active patients	1	
Determine study status from list	1	study is open
Multiply (number of patients * the Protocol Workload Score) *study status = Case Workload Score	8	
Step 3:		
Add Protocol Workload Score + Case Workload Score= Total Workload	16	

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A New Era of Complex Trial Designs

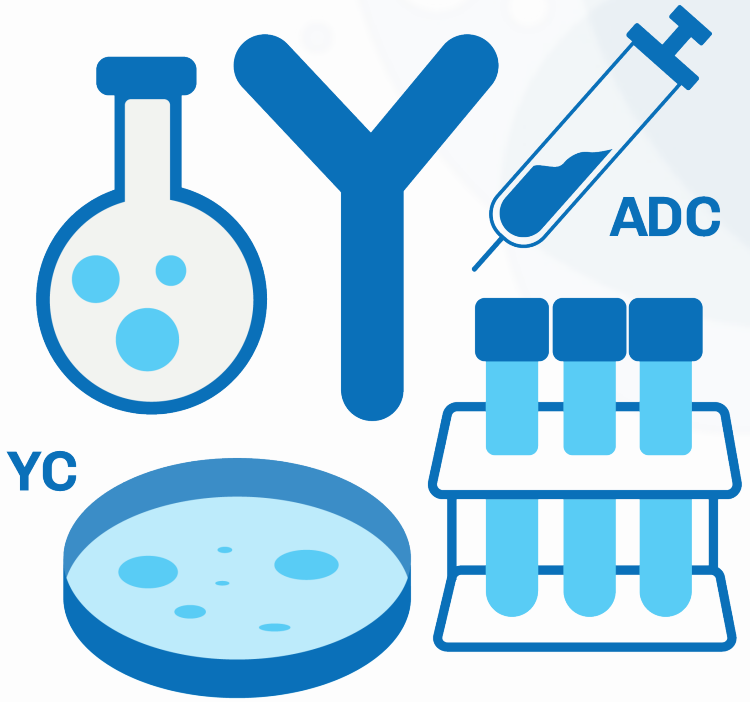
…Meeting the challenges ahead

Presented By: Jenny Keppler

Industry Trend: Complexity is persistent and intensifying

Major Factors Driving Trial Complexity

- Recent Regulatory Guidance mandating or "encouraging" change
- The "promise" of innovative study designs to reduce drug development time
- Scientific advancements, leading to:
  - *New, complex classes of drugs*
  - *Innovative technologies for new biomarkers for eligibility or therapy response*



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New regulatory expectations and opportunities

New FDA Guidance Catalyzes Change

- Mandates to expand trial populations
  - Clinically relevant patient populations are in the study
  - Inclusion of older patients, ethnically diverse, and chronic disease populations complicate study operations
    - Additional PK assessments
    - Dose modifications
    - Selective recruitment of certain populations

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It is important to meet these challenges head on…

FDA Initiatives will be Slow to Change (if ever)

- Initiatives expanding trial populations
  - *Obtain recruitment tools and funding* from sponsor to address needed demographics
  - *Staff the study as designed not as "labeled"*
    - Is enrollment adaptive?
    - Are there dose escalations / de-escalations for elderly or chronic disease?
    - Stratification to arms with different assessments (e.g., PK, safety labs, etc.) ?
  - *Sponsors may consider sub-studies* for sites equipped for higher risk patients (e.g., DDI)

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Innovators develop, followers adopt, FDA guidance emerges

Innovative Designs to "Expedite Timelines"

- New Dose Escalation Paradigms (oncology primarily)
  - Simple "rule-based" designs are being replaced
    - Model-based or model-assisted designs enroll more patients and may be harder to understand next dose
    - Adaptive backfilling of "safe-doses" is an additional complexity
- Multiple Expansion Cohorts (oncology primarily)
  - Essentially multiple clinical trials, within a single protocol
  - Efficient testing of populations or combination regimens
- Adaptive Trial Designs
  - Significant change can be based on emerging evidence or interim analyses

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Some "winning approaches" will emerge…others will fail

Innovative Designs will Settle into a New "Normal"

- Complicated dose escalation paradigms and backfilling
  - Request schematic from sponsor to show decision points and enrollment slots
- Staff "Multiple Expansion Cohort" studies to meet operational demands
  - Separate internal study documentation by cohort, including patient consents, trackers, checklists, etc.,
  - Manage divergent arms as if they are separate studies
- Adoption of the more complex adaptive trial designs will depend on success
  - Plan for multiple protocol amendments and the resulting operating burden
  - Consider the impact of multiple interim analyses and consider staff supplementation

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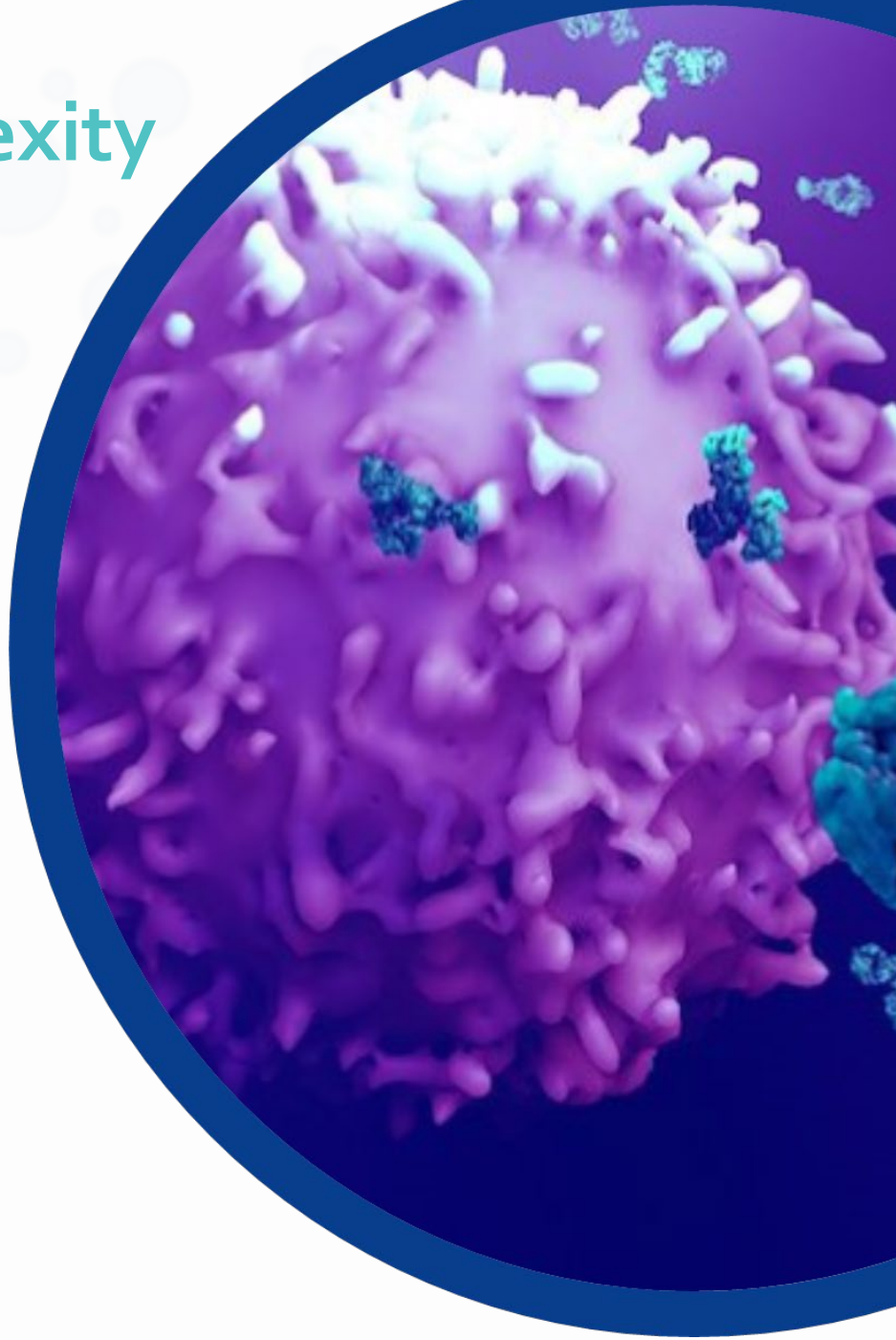
Technological growth and trial complexity

May Have Exponential Impact

- New classes of treatments require new thinking
  - Increased assessments impact patient & site burden
  - Different adverse event profiles and timing
- The Sponsor's View – new technology is good!
  - Genomic-based criteria are now an option
  - Technology advancements offer a lot of new options often without clarity on optimal assessment or timing
    - Sponsor: Let's do them all and at every timepoint!
- Site's (and Patient's) View – Oh No! *Another test?*



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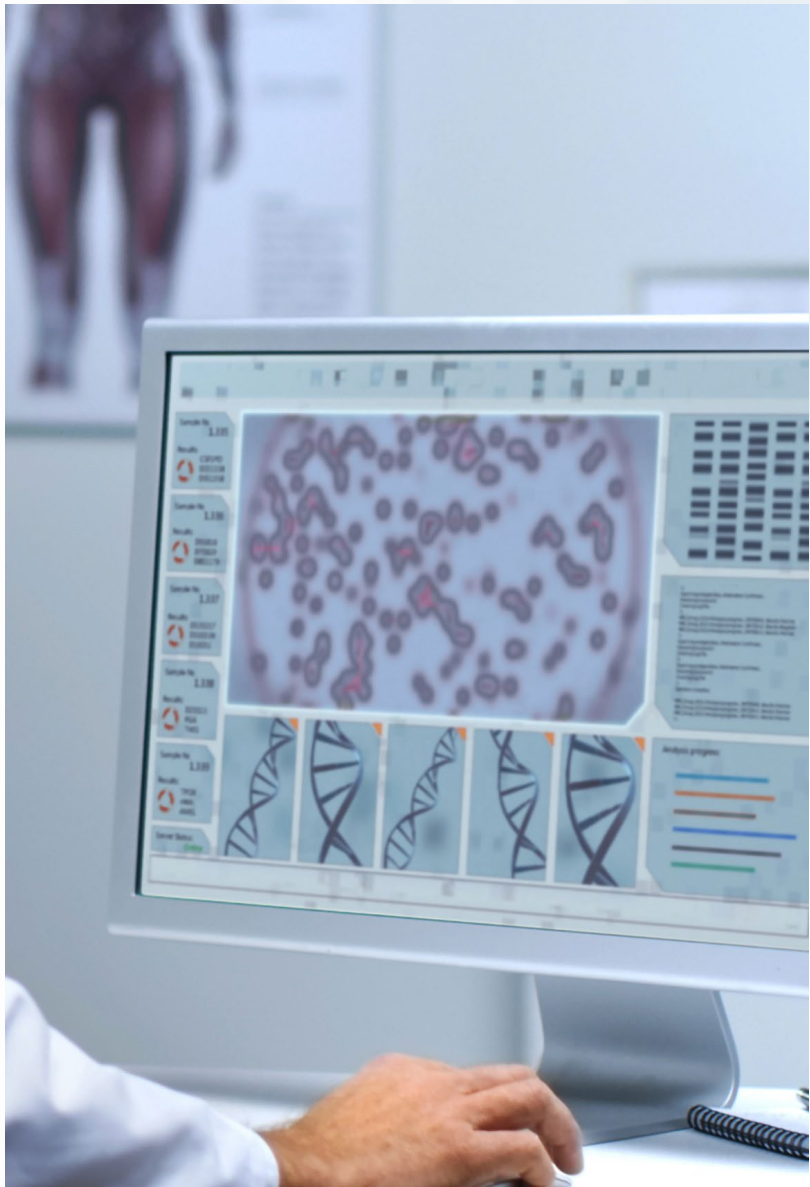
Coping with the status quo, until new standards are set

New Drugs and Technologies

- If possible, get involved early with the study before protocol is finalized
  - PI to advise on study design and prevent assessment overload
  - Study team to identify logistical challenges
- Carefully evaluate staffing requirements, especially for study visits, scheduling, and specialized lab/tissue processing
  - Develop matrices for study visits and sample processing to layout staff needs by function
  - Prepare more detailed study-visit checklists or flow charts



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Industry Trend: Complexity is persistent and intensifying

Adapting for this Trend is Key to Success

- Plan for new studies to be complex, for now:
  - Develop study assessment tools and matrices to effectively assess resourcing for the study
    - *Consider how staffing will flex during trial visits and overall study* (e.g., sample processing, interim analyses, etc.)
    - *Consider time needed to develop* more detailed checklists, multiple consents (as relevant), and study flowcharts
  - Work with the sponsors to:
    - *Meet your site's needs,* for schematics and flowcharts, etc.
    - *Provide recruitment tools and funding* to meet enrollment needs for diversity goals

A *new balance* between new designs and assessments with information yield and study success will emerge

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Panel Discussion & Audience Questions

Polling Question #3:

Would you be interested in providing input on your amendments process for WCG's upcoming Amendments Project?

Please select yes if interested and we will follow-up with you!

Don’t Forget to Register for Parts 2 and 3 of our 2024 Site Challenges Webinar Series!

Part 2: Recruitment & Retention – November 21st
Part 3: Study Start-up – December 12th

wcgclinical.com/events

Download WCG's 2024 Clinical Research Site Challenges Report Today for Free!

www.wcgclinical.com/challenges

Polling Question #4:

Are you interested in learning more about WCG's Site Enablement solutions for sites or Study Planning solutions for sponsors/CROs?

Thank you!

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