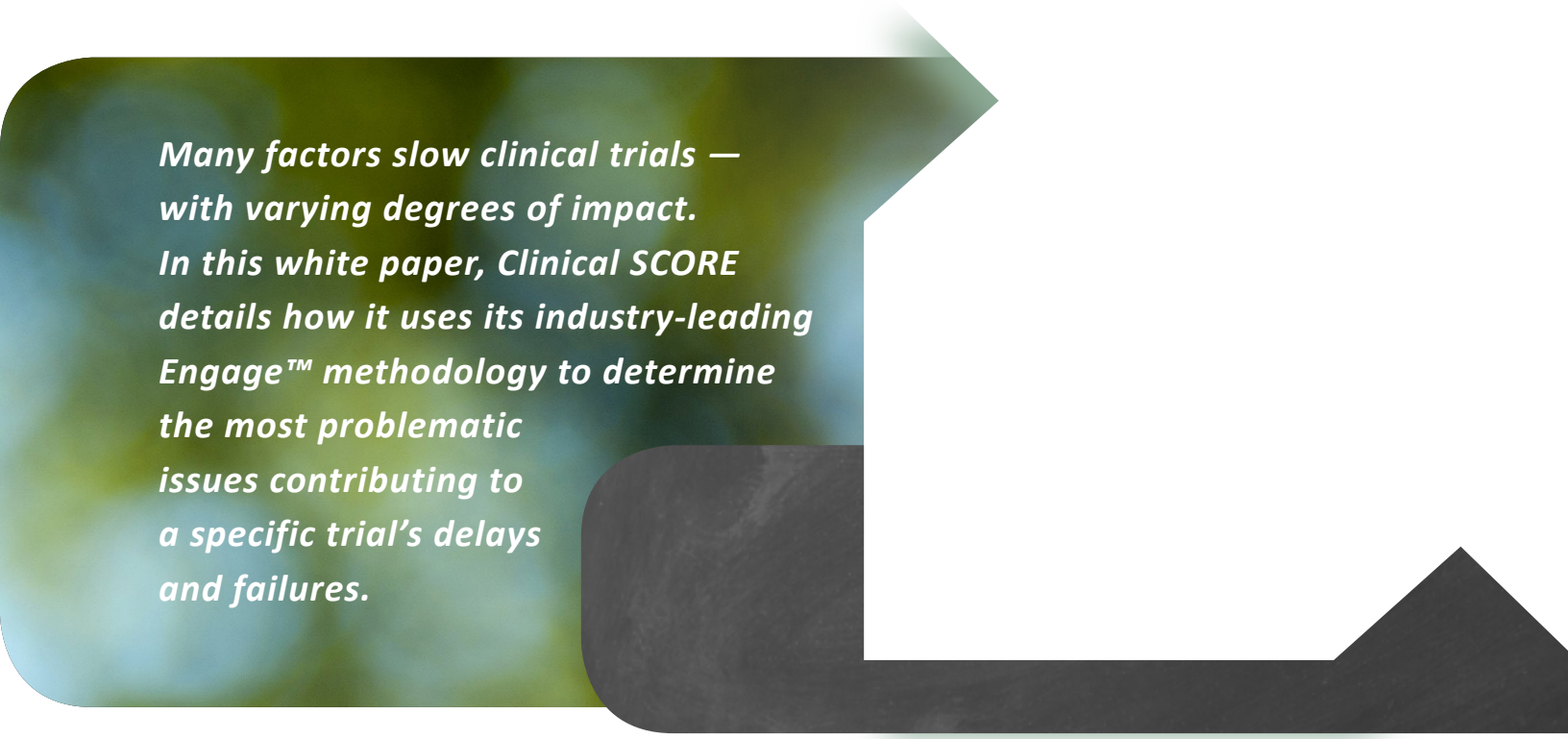
ARE WE IGNORING THE PITFALLS OF INNOVATIVE CLINICAL TRIAL TECHNOLOGY ADOPTION?

Pinpointing Roadblocks to Timely Study Completion



Many factors slow clinical trials — with varying degrees of impact. In this white paper, Clinical SCORE details how it uses its industry-leading Engage™ methodology to determine the most problematic issues contributing to a specific trial's delays and failures.

CLINICAL SCORE

EXECUTIVE SUMMARY

It is widely known that clinical trials face issues with efficiency and quality, and many biopharmaceutical enterprises and CROs are implementing programs to minimize these risks. For example, the emergence of risk-based monitoring (RbM) and eSource to mitigate data quality risk, to patient matching technologies that improve enrollment efficiency[7], through eConsenting to enhance the delivery of information to patients and generate insights on patient behaviors, are signs that the industry is piloting and adopting a culture of technology innovation[8]. Despite these advancements in clinical trial technologies, many studies are delayed, or go over budget because they **ignore the human relationship element in clinical operations**, which involves bridging the communications gap between patients, study sites, CROs and the Sponsor while rolling out these new technology pilots.

Clinical SCORE's **Engage™** methodology is scientifically designed to accelerate clinical studies by identifying issues that are hindering the completion of a study, comparing results against a benchmarked database of more than 200 successful studies, and delivering actionable recommendations based on qualitative and quantitative input from the Sponsor's own investigators and coordinators. Clinical SCORE developed a two-step research program to validate the methodology and identify areas of major concern common to most clinical trials.

After extensive interviews and analysis of data from sites around the world, Clinical SCORE uncovered that **clinical trial software is the major contributor to clinical trial delays**. Further, the researchers identified specific software-related issues that hinder trial success.

Having knowledge of specific roadblocks in a given trial positions the Sponsor to initiate targeted solutions to address these barriers and keep the trial on track. The research indicates that Engage™ provides a valid methodology for identifying critical impediments, enabling Sponsors and CROs to create solutions that address these issues before they become irreversible impediments that introduce exponential risks towards timeline slippage.

THE IMPACT OF BEING OFF TRACK

The pharmaceutical industry faces financial pressures to rapidly bring a new drug to market — ranging from $160 million to more than $2 billion.[1,2] These delays can result in a range of $600,000–$8 million per day in lost revenue opportunities,[3,4,5] and create crucial setbacks in the availability of new medications to patients. In light of this, it is critical that sponsors identify and address roadblocks promptly.

In addition to pressures affecting timeline delays, some of the factors driving the need for greater clinical trial efficiency include:

- **The need to manage numerous simultaneous trials within a complex system of global compliance regulations**, particularly since the US Secretary of Health and Human Services delegated monitoring authority to the US Food and Drug Administration (FDA) in 2012
- **Vast changes in the business environment**, including an increase in outsourced partnerships and mergers and acquisitions
- **Extensive innovation** in biomedical research, genomics and medical technology

The industry has explored a number of advancements aimed at minimizing timeline slippage and trial duration. These range from best practice groups and adaptive trial designs to use of electronic medical records (EMRs) to identify eligible patients and recruitment updates using interactive web-based platforms to obtain informed consent. Despite these and other advances, the National Institutes of Health (NIH) reports that 80% of trials in the United States fail to meet their recruitment or enrollment estimates.[6]

Ironically, the very tools that are chosen to streamline study enrollment, data collection and other tasks are often the source of the problem. For example, problems related to software — password management, slow performance, lack of support — can frustrate clinical site personnel and impede the trial. These roadblocks are not always obvious to the Sponsor or study coordinator. Fortunately, Clinical SCORE has developed a process to identify and address these and barriers to timely clinical trial completion.

Over **$2 billion** to introduce a new drug to the market.

Because of delays, **$8 million** per drug can be lost to Pharmaceutical Companies if clinical trials results aren't delivered on time.

80% of clinical trials in the United States don't meet their timelines.

VALIDATING THE PROCESS

To identify micro-level issues that create roadblocks to clinical trial success, Clinical SCORE took an approach that is novel in the clinical trials industry, eliciting opinions from medical professionals on the clinical trial front lines: principal investigators (PIs) and study coordinators (SCs) at sites worldwide.

Step One: Exploratory Research Clinical SCORE conducted 25 in-depth, hour-long interviews with PIs and SCs, in person and over the telephone. The objectives were to:

- Identify all issues that the subjects had encountered during their tenure as PIs or SCs that could impact clinical trials
- Include these issues in the Step Two survey document

The net result was a list of 125 issues that impact clinical trials to varying degrees.

Step Two: Quantitative Research Based on the issues identified in Phase One, Clinical SCORE conducted online quantitative surveys of PIs and SCs from the Clinical SCORE database. This database contains clinical trial sites including:

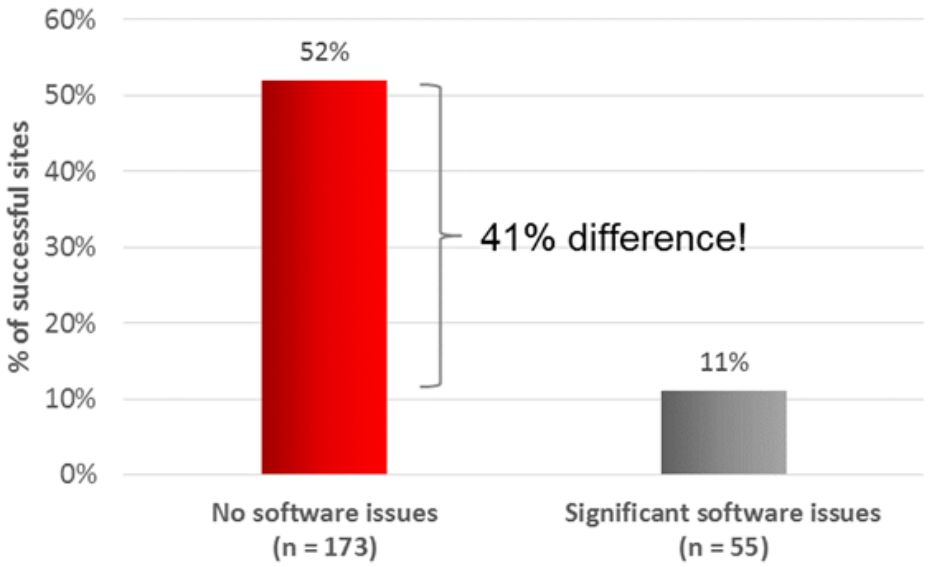
- 25 countries worldwide
- 28 medical specialties
- All major research types (academic, large clinical, small clinical, dedicated research and non-academic hospital)

The final results reflected the outcomes of 403 unique clinical trials and elicited a response rate of 55%. Opinions were solicited from both PI's and SC's. Sites were divided into two categories: **Successful sites** randomized 75% or more of the subjects they initially believed were feasible; **unsuccessful sites** randomized less than 75%. To determine the greatest impediment to success, Clinical SCORE:

- Compared category means
- Compared issues among sites with significant problems
- Analyzed open-ended responses

PINPOINTING THE PROBLEM

Each trial had its own set of unique problems, which prevented success and created delays of various degrees. Roadblocks included clinical research associate (CRA) turnover, lack of adequate training, investigator meeting deficiencies and problems with the central lab. However PIs and SCs indicated that the issue that most prevented the success of a clinical trial at their site was software. Of the 403 sites interviewed, 97 (24% of the total) had major software problems — rated 8 or higher on a 0- to 10 scale; 86 of the sites with software problems did not succeed. Sites with no software issues were more likely to be successful than sites with significant software problems.



More than half (52%) of sites with no software issues were successful, compared to only 11% of sites with significant software issues.

Type of Site	Mean Number of Active Trials
Academic	18.4
Large Clinical	13.5
Small Clinical	7.9
Dedicated Research	14.8
Non-Academic Hospital	19.7

Considering the number of ongoing active trials at different types of sites at any given time, the negative impact that software problems can have on SCs' ability to complete their jobs is clear.

Qualitative and quantitative analysis uncovered specific software issues that impacted trial length and sometimes led to failure. These ranged from inconsistent electronic data capture (EDC) fields to unclear queries. It is important to note that complaints about software and passwords existing during almost every trial, but when they reach significant proportions, they stand in the way of a trial's success.

Software Issues	Successful Trial	Unsuccessful Trial
Queries were Unclear	22%	78%
EDC Data Entry Input was Confusing	27%	73%
Software Crashed Too Frequently	32%	68%
Passwords Changed Too Frequently	41%	59%
Too Many Passwords	41%	59%
Data Entry Repetitive	41%	59%
Inadequate Training for Software	42%	58%
Excessive Queries	44%	56%
Inadequate Training Manual	46%	54%
Sponsor Portal was Inefficient	47%	53%
EDC Data Fields were Inconsistent with Data Required	47%	53%

Granular analysis identifies specific problems with software and their prevalence in successful and unsuccessful trials.

Feedback from respondents

Can the passwords be coordinated? Why is it necessary for some trials to be so difficult simply because of the passwords? (US SC)

If there is any way to make the EDC database faster, it would improve the efficiency of data entry and query responses. (UK SC)

Something happens and nobody knows who to call because there are so many vendors. (German SC)

The trial uses way too many software systems. (UK SC)

Offshore support is not always available. (UK SC)

Too many changes to data entry program with no notice of change. (French SC)

There seem to be a lot of portals/electronic systems for this study. It adds weeks to the trial. (US SC)

If they want one reason why the trial takes so long, it is because there are way too many vendors. They each have their own systems. (Spanish SC)

It becomes difficult to waste my SC's time. They seem to wait for hours dealing with software problems. I tell them to move onto another trial. (US PI)

THE SOLUTION: THE ENGAGE™ DASHBOARD

A great deal of time, effort and capital go into researching novel therapies and creating study protocols to test them. Software issues play a major part in clinical trial delays and failures. Proactively identifying specific issues allows study teams to initiate procedures that eliminate the roadblocks. These can include:

- Ensuring that software adequately matches protocol requirements
- Ensuring that CRAs are fully trained on all software
- Enhancing CRA and Data Manager training on communications clarity with managing queries in EDC
- Managing emails generated from software vendors
- Requiring full software training before a replacement CRO can initiate responsibilities
- Providing access to software for password management

Using an independent and objective third party to assess possible roadblocks in real time can provide a platform to address these barriers, increase operational efficiencies and keep trials on track.

The Engage™ methodology and benchmarking system from Clinical SCORE provides a systematic way to collect data in order to identify high-level issues and granular detail about the specific factors impacting a trial, using a validated tool that compares results with successful trials to gauge trial performance. In two weeks' time and for a minimal investment, **Engage™** evaluates more than 120 potentially problematic issues and identifies the areas your PIs and SCs need you to address to accelerate your trials. After all, successful sites lead to successful trials.

To engage your sites and accelerate your trials, contact Ross Weaver at (877) 334-0100 or email Ross.Weaver@clinical-score.com.

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Gary Kaplan is director of research and analysis for Clinical SCORE. His main areas of expertise are sample design, study design and data analysis. He has extensive experience, having spearheaded and directed survey research in more than 15 industry sectors, including commercial pharmaceuticals, operational pharmaceuticals, converged technology (IT and telecommunications), expedited shipping and political polling. He has served as director of analysis at Consumer/Industrial Research Services, chief statistician at Chilton Research Services, director of the Advanced Methods Group at TNS US and the US director of Leger Marketing. Mr. Kaplan has presented design approaches and survey results worldwide to audiences in 20 countries and at academic institutions including McGill University, Montreal, Canada; Emory University, Atlanta, Georgia; and the University of Washington in Seattle. His articles have appeared in Advertising Age, the Journal of Marketing Research and Quirks Marketing Research Review, and he has authored white papers for the Advertising Research Foundation. He holds a Bachelor of Science degree in psychology and a Master of Science degree in urban studies, both from Tulane University in New Orleans, Louisiana, and a Master of Science in applied statistics from Temple University, Philadelphia, Pennsylvania.