

WHITEPAPER

BETTER ADHERENCE, HIGHER ENGAGEMENT: FINDING THE CLINICAL TRIALS SWEET SPOT



SPENCER HEALTH SOLUTIONS

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INTRODUCTION

Clinical trial sponsors and clinical research organizations must work through an ever-expanding set of challenges to ensure their studies of new drugs produce valid results. And they must do so while strictly managing costs and timelines. As more trials make use of in-home settings, digital technologies and real-time patient data, the pressure increases to efficiently manage a process that's dramatically different from the traditional methods of direct observation inside the walls of a clinic.

Sponsors are increasingly considering new technology to help them manage trials in this fast-developing environment. Technology platforms, digital applications, electronic patient diaries, wearables, data sharing, videoconferencing and various forms of artificial intelligence are among the many new methods with the potential to reduce time and cost associated with trials.

And yet, adoption isn't where it could be. According to the Deloitte Center for Health Solutions, the industry has been slow to update clinical trials processes with digital capabilities.¹

This is now changing as organizations see the potential for patient-centric digital technologies to transform clinical development.

The increasing focus on modernizing clinical trials raises questions about where sponsors should invest their resources. Is it in tools to expedite patient recruitment and retention? Improve data collection and reporting? Increase patient engagement? Reduce non-adherence?

Adherence has a significant impact on patient retention.

Non-adherence and lack of engagement are known to play a significant role in whether a patient finishes a study or drops out. With respect to patient engagement, increased engagement between physicians and trial participants has been found to have a significantly positive correlation with adherence.² Thus, sponsors are striving to utilize different strategies and technologies to enable participants to accurately report their health status.

Medication adherence is one of many essential considerations for clinical trial sponsors and CROs as they move from study design and patient recruitment to the study itself and data analysis. Non-adherence in particular has been shown to increase variance, lower study power, and reduce the magnitude of treatment effects.³

A close-up photograph of numerous blue and white capsules scattered on a white surface.

THE ROLE OF ADHERENCE AND ENGAGEMENT IN CLINICAL TRIALS

Much is at stake: By reducing non-adherence by just one percentage point, sponsors can save an estimated \$335,000 in the total cost of a Phase III trial as a result of needing to recruit and retain fewer participants to preserve statistical power.⁴

Causes of non-adherence are diverse but include lifestyle disruption, side effects, or they may simply forget to take their medication. When participants are actively engaged during the medication process and take their medications as prescribed during the trial, it reduces a host of worries for sponsors.

Concerns include the quality of the results, the cost of the study and the extra patients needed to be enrolled to replace any dropouts.

To assess the impact that medication adherence plays on clinical trials, Exploristics, a trial design and analysis firm, partnered with Spencer Health Solutions to **conduct hundreds of simulated hypertension studies to measure the impact adherence may play on a hypertension clinical trial.**

Simulations are important and relevant to clinical trials. The FDA promotes modeling and simulation as an advancement in the clinical trials process that can help bring therapies to market more quickly and effectively. In fact, the agency regularly advises industry to use modeling and simulation to predict outcomes from clinical trials, inform trial design, and support evidence of effectiveness, among other reasons.⁵

MEDICATION ADHERENCE DEFINED

The World Health Organization defines adherence as the degree to which patients' behavior aligns with the recommendations of a health care provider. When patients comply with those recommendations at least 80 percent of the time, they're considered adherent.

PATIENT ENGAGEMENT DEFINED

The Patient-Centered Outcomes Research Institute (PCORI) has established a definition of patient engagement for clinical research: "The meaningful involvement of patients, caregivers, clinicians and other healthcare stakeholders throughout the entire research process - from planning the study, to conducting the study, and disseminating study results."

The Spencer Health Solutions-Exploristics Simulation: Modeling a Hypertension Clinical Trial

Clinical trial simulation involves the use of a model to describe a process or system, executing the model, and analyzing the outputs. Simulation is useful when there are multiple, interrelated factors that impact the outputs.

The Spencer-Exploristics simulation was designed to estimate the impact of adherence on the probability of success in a trial of a hypertensive population with a high risk of stroke. A stroke study, published in *The Lancet*, was used and represented a randomized trial of 6,105 individuals with previous stroke or transient ischemic attack. This study was chosen because hypertension is a chronic condition and this study allowed for reasonable assumptions to be made regarding the impact of adherence on stroke.

The underlying model for the simulated studies comprised the following factors:

- Risk of stroke in placebo control group
- Risk of stroke in treated population
- Proportion of subjects with non-adherence in a study
- The extent of non-adherence in the clinical trials population
- Risk of stroke in subjects given their adherence

The simulations enabled an evaluation of the performance of different study designs under different compliance scenarios. The scenarios included studies with sample sizes ranging from 500 to 1,900 patients equally allocated to an active treatment arm and a control group. Ten scenarios relating to compliance were defined by the combination of the proportion of subjects with non-adherence and the extent of non-adherence. Results from three of the scenarios are reflected in the charts on the following pages.

For each compliance scenario and sample size, 500 simulations were run by generating virtual patient-level data that conforms the assumptions defined by each scenario. Once the data was generated, the proportion of patients with stroke in the active treatment group was compared with the placebo group using a Chi-squared test and the comparison was declared significant at the 5% level. The percentage of simulations that achieved significance then gave the probability of success for each scenario. The target sample size for each compliance scenario was determined by the value that achieved a probability of success between 80 and 90%.

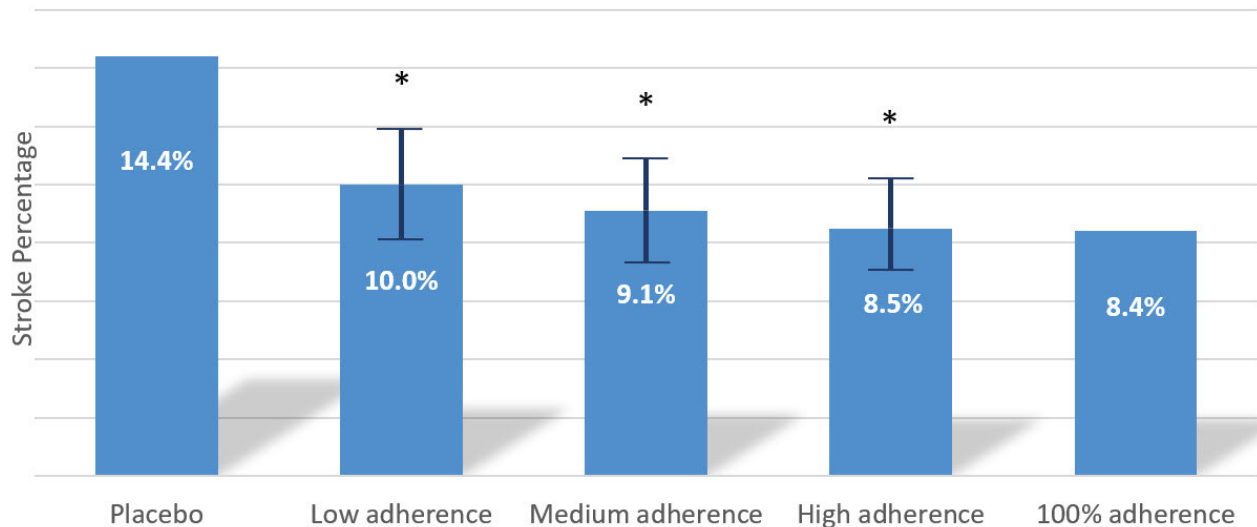


After all simulations were completed, two findings stood out:

First, changes in adherence make a substantial difference in patient outcomes.

The graph below summarizes the probability of stroke for all 500 simulations with increasing levels of adherence compared to the published placebo control and treated results from the original study.

Low adherence increases the likelihood of Stroke by 42%



*Simulated results. Error bars represent entire range of simulation.

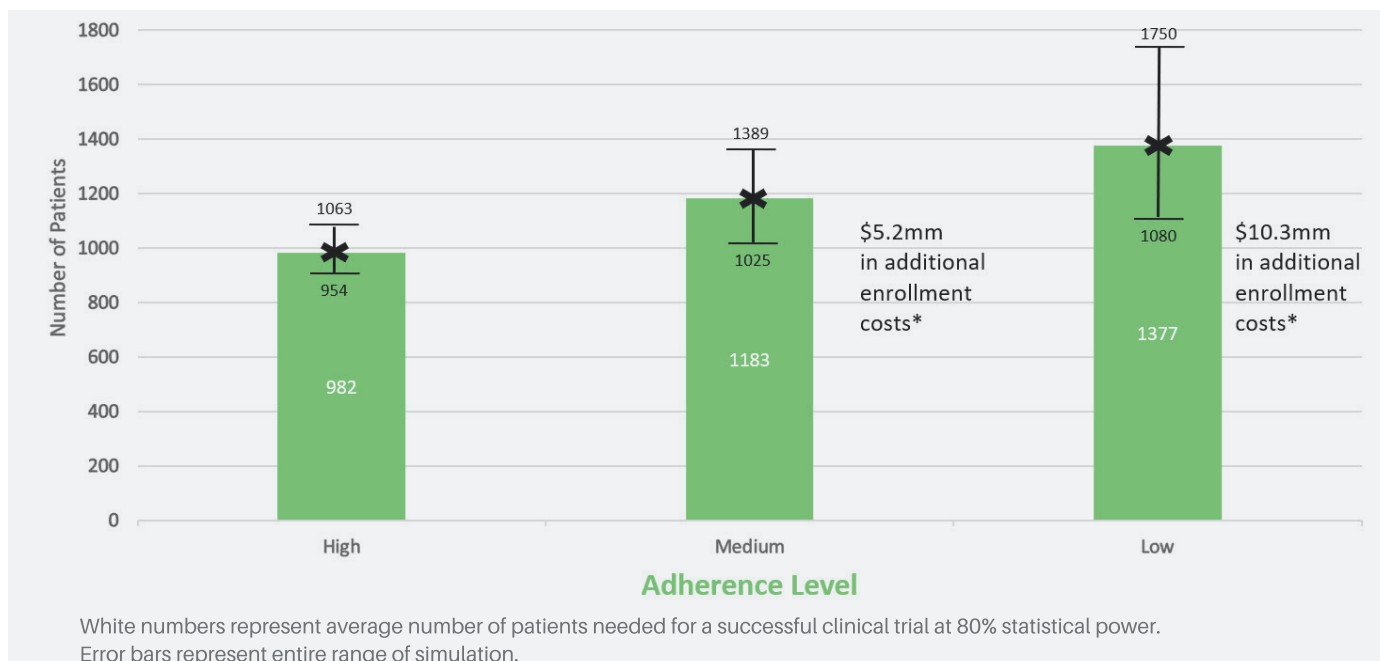
For example, at an adherence rate of 70 percent, 10.3 percent of trial participants would be expected to experience a stroke within four years. But when the adherence rate climbs to 90 percent, just 9.1 percent of patients would be expected to experience a stroke. (The placebo stroke rate after four years was expected to be 14.4 percent.)

MEDICATION ADHERENCE: A SIGNIFICANT INFLUENCE

Second, low adherence dramatically increases the number of trial participants needed to achieve valid results.

The chart below shows that 1,183 subjects would need to be recruited and enrolled at a 70 percent adherence rate (for 70 percent of participants). At 90 percent adherence (for 90 percent of participants), the number of subjects needed falls to 982, a decrease of 201 patients needed for recruitment.

Low adherence requires an additional 40% increase in patients needed for a successful trial.



These findings demonstrate that adherence accounts for a larger role in trial efficacy and likely outcomes than is generally believed. If an increase in adherence of 10 to 20 percentage points means fewer participants need to be recruited and engaged to completion, the implications on costs and timelines can be substantial.

For example, an analysis published in Applied Clinical Trials estimated the average cost of enrolling one patient in a Phase III trial at \$26,000.

Thus a typical hypertension study may realize up to an additional \$10.3mm in patient enrollment expenses when comparing the low to high adherence scenario.



SUMMARY

ADHERENCE AND ENGAGEMENT: TAKING CENTER STAGE

The findings from our simulations show that adherence has a substantial impact on the cost, efficacy and likelihood of success in clinical trials. For example, **the number of patients needed to complete a study with a statistical power of 80% nearly doubles when non-adherence is 40 percent**, compared to full adherence. These findings have important implications for sponsors as they search for the right technologies and methodologies to modernize their trials.

The transformation of clinical trials is here to stay. Traditional research and development processes are being modernized, the regulatory framework is embracing digital technologies, and – perhaps most important – patients are being given a real voice as stakeholders in clinical trials. These changes are necessary as pharmaceutical, device, and life sciences companies face intense pressure to deliver safe, effective therapies at a greater value to consumers.

CASE STUDY: SPENCER HEALTH SOLUTIONS

95%

medication adherence

81%

patient engagement

Patients using a spencer device in the home showed a 95% medication adherence rate of medications taken during time prescribed. Those same patients provided feedback through the device 81% of the time when asked a question, averaging 2.5 questions daily. Measures taken 2017-2019 from pilot with 160 patients (average age 70 and each with at least one chronic condition) using spencer device in the home.

Citations:

- 1 Deloitte Center for Health Solutions: <https://www2.deloitte.com/insights/us/en/industry/life-sciences/digital-research-and-development-clinical-strategy.html>
- 2 Med Care: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2728700/>
- 3 Journal of Clinical Pharmacology: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5066799/>
- 4 Applied Clinical Trials: <http://www.appliedclinicaltrials.com/non-adherence-direct-influence-clinical-trial-duration-and-cost>
- 5 FDA: <https://www.fda.gov/science-research/about-science-research-fda/how-simulation-can-transform-regulatory-pathways>

AUTHORS



Alan Menius is the Chief Scientific Officer at Spencer Health Solutions. He is responsible for developing the scientific strategy for using the spencer SmartHub in clinical research as well as leveraging spencer data. Prior to this role, Alan spent 25 years at GlaxoSmithKline where he led advanced analytics teams responsible for leveraging disparate data sources and advanced analytics to inform the safety and effectiveness of medicines. Alan has over 20 publications in peer-reviewed journals and has given numerous invited presentations on advanced analytics at national and international meetings.

Aiden Flynn is the founder of Exploristics and has more than 20 years' experience in drug discovery and clinical development. After seven years as a lecturer at University College, London, he spent ten years at GlaxoSmithKline as a director of statistical support for biomarker studies across research and development. He was responsible for developing and implementing the pharmacogenetics strategy that enabled the use of genetics data in clinical studies. This involved the integration of a wide range of capabilities across R&D such as new analysis tools and methods, bioinformatics, data standards, processes and training. In recent years, Aiden has worked closely with regulatory authorities, such as the FDA and EMEA, to develop tools and guidelines that support the use of biomarkers in clinical studies.



About Exploristics

Exploristics provides analytics, statistics, exploratory data analysis, modelling and simulation services. They have unique expertise in handling large data resources, including Clinical Trials, Biomarker, Pharmacogenomic, Imaging and Observational data.

About Spencer Health Solutions

Advancing research and healthcare from the home. Spencer Health Solutions, Inc. leads the digital health market with the spencer® Smart Hub. Bring new treatments to market faster and at a lower cost with the award-winning spencer, which combines medication dispensing, telehealth and engagement, so patients, their healthcare providers and clinical research teams stay connected.