

White Paper

# Finding value in failing trials

*How AI-driven platforms can save failing trials by using data to validate results, hone protocols, identify sub-populations with shared traits, and ensure the right patients are recruited to demonstrate success.*

**KAL CHAUDHURI**, MBA, Principal, Sub-Population Optimization and Modeling Solutions, IQVIA

**RUSSELL REEVE**, PhD, Vice President, Decision Sciences, IQVIA

**ADRIAN McKEMEY**, PhD, Senior Vice President, Consulting Services, IQVIA

**PENNY RANDALL**, MD, MBA, Vice President and Head, CNS Center of Excellence, IQVIA



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# Executive Summary

Failed clinical trials can cost sponsors more than a billion dollars, and waste years of time developing a drug that will never get to market. However, these losses can now be mitigated through the use of artificial intelligence (AI) and machine learning-driven platforms that identify sub-populations of patients within a clinical trial who could respond positively to a treatment.

When sponsors can find these populations and adapt the trial design accordingly, it can reduce the rate of trial failure, rescue a promising molecule for further development, and capture better primary and secondary endpoint data to support approval and payer valuations.

This paper explores how sponsors can leverage AI driven tools, such as IQVIA's Sub-Population Optimization and Modeling Solutions (SOMS), throughout the trial lifecycle to reduce the risk of failure, while improving success rates, and identifying new opportunities in drug development.

## **PART 1: THE HIGH COST OF FAILURE**

The enormous cost of drug development is caused in large part by the high rate of failure. A 2019 study found that less than 14 percent of all drug development programs eventually lead to approval, and that number drops to just six percent for orphan drugs, and a mere 3.4 percent for oncology drugs, which is a dominant category for drug development.<sup>i</sup>

When trials get shut down, sponsors face enormous financial losses — an estimated \$800 million to \$1.4 billion<sup>ii</sup> — and patients lose the hope of potentially lifesaving treatments coming to market.

While some molecules simply don't pan out, many trials fail because the trial design did not adequately identify the appropriate population, endpoint, and/or dose selection. This can result in a majority of trial participants not responding as hoped, or adverse events occurring that make safety risks too high. However, with the right data, this high rate of failure doesn't have to occur.

Within failed trials, there are often sub-populations of patients who respond well to the treatment and suffer no adverse events, but because the overall numbers don't add up, the trial is abandoned. This means sponsors lose their investment and patients who could potentially benefit from lifesaving treatments are denied these innovations.

These populations can be identified through the use of SOMS platforms, which leverage AI and machine learning tools that can rapidly analyze clinical data sets to identify the most promising populations, allowing sponsors to adapt the trial accordingly. When sponsors can identify these sub-populations sooner in the research process, they can adapt the trial to focus on those patients. This increases safety and treatment outcomes through better trial design and can rescue promising trials that would otherwise be deemed failures.

i <https://academic.oup.com/biostatistics/article/20/2/273/4817524>

ii <https://www.clinicalleader.com/doc/the-high-price-of-failed-clinical-trials-time-to-rethink-the-model-0001>

## Part 2: How the technology works

These statistically rigorous analytical platforms feature machine learning algorithms that are programmed to analyze trial data to identify predictive biomarker(s) in treatment populations who are experiencing stronger outcomes. They can be used at various points in the trial lifecycle to identify trends and outliers without bias, to inform trial design, support approval and pricing decisions, and shape market and sales strategies.

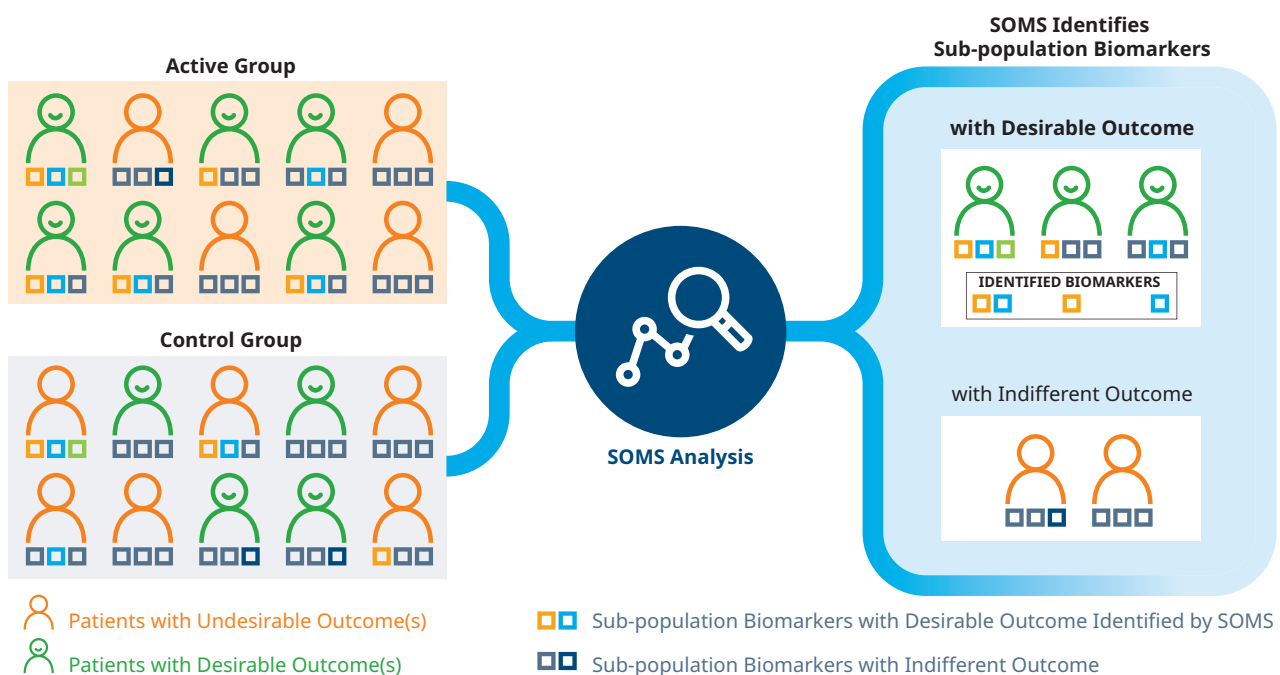
The platform utilizes an industry recognized analysis method called Subgroup Identification based on Differential Effect Search (SIDES). SIDES is used to evaluate trial results to help clients answer tough questions about the effectiveness of a drug in development, and to develop effective trial design strategies to maximize their chances of success. These platforms use secure data management technologies

and intuitive workflows that automatically query patient data sets based on predetermined features, and deliver results in easy-to-read charts, scatter plots, and summaries.

The easy to read graphical interface allows stakeholders to quickly review and understand which patient populations are responding to the treatment, who among them are facing a higher risk of adverse events, which populations are not likely to benefit, and where there are cut offs. For example, an analysis might show in a series of graphics that patients over the age of 65 with stage three cancer are more likely to respond to the treatment than younger patients, and that those in earlier stages of the cancer have a higher rate of adverse events.

### How SOMS Works?

SOMS is a statistically rigorous machine learning analytical platform that can identify predictive biomarker(s) in treatment populations with stronger outcomes by analyzing multiple biomarkers simultaneously



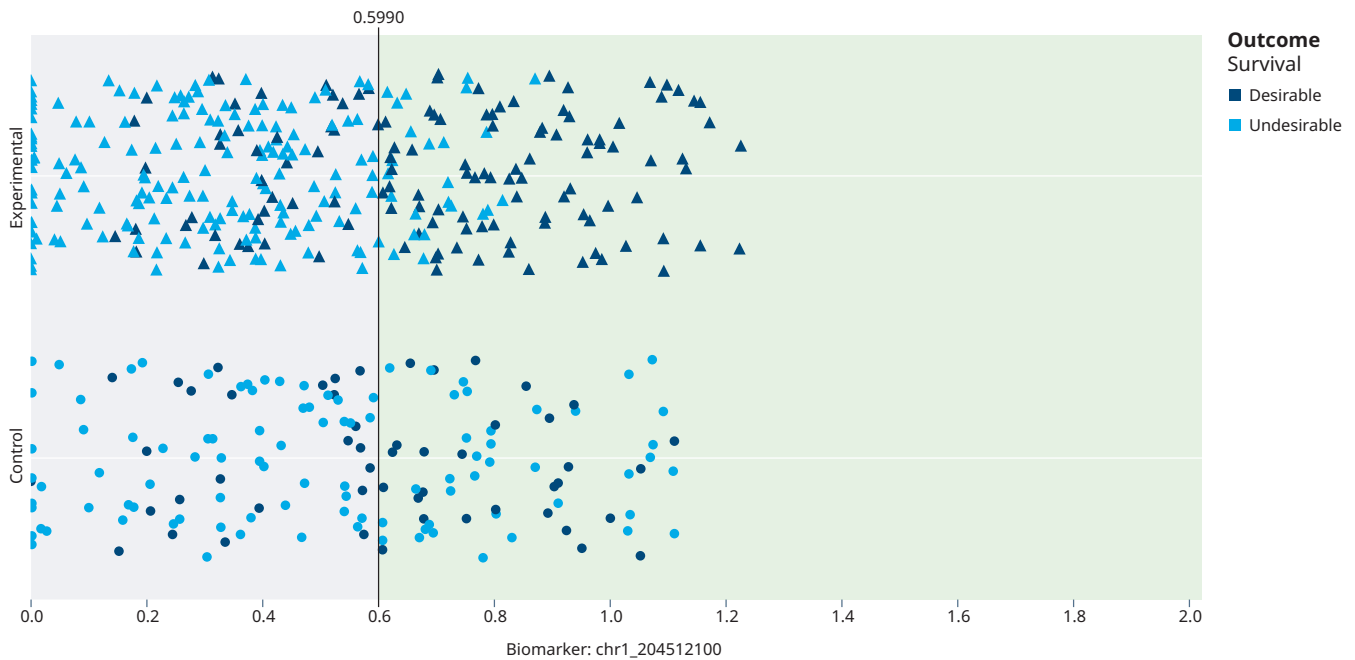
This kind of instant easy to understand data gives investigators and sponsors the insights they need to adapt the trial and select the right patients with greater precision and confidence. That can reduce time, cost and risk across the trial lifecycle, from early discovery through commercialization, and enable sponsors to bring more successful treatments to market.

These platforms deliver value at many stages of the trial lifecycle from early stage decision making, through approval, market access and extension studies.

And when the data shows that no population is having meaningful outcomes, this technology can also save sponsors hundreds of millions of dollars by shutting down failing trials sooner and moving those resources to molecules that have a greater potential of generating returns.

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**Artificially generated data to identify sub-population based on % of cells showing mutation of Chromosome-1 at position 204512100.**



Source: IQVIA Sub-Population Optimization and Modeling Solutions (SOMS) Platform

### PLANNING FOR PHASE 3

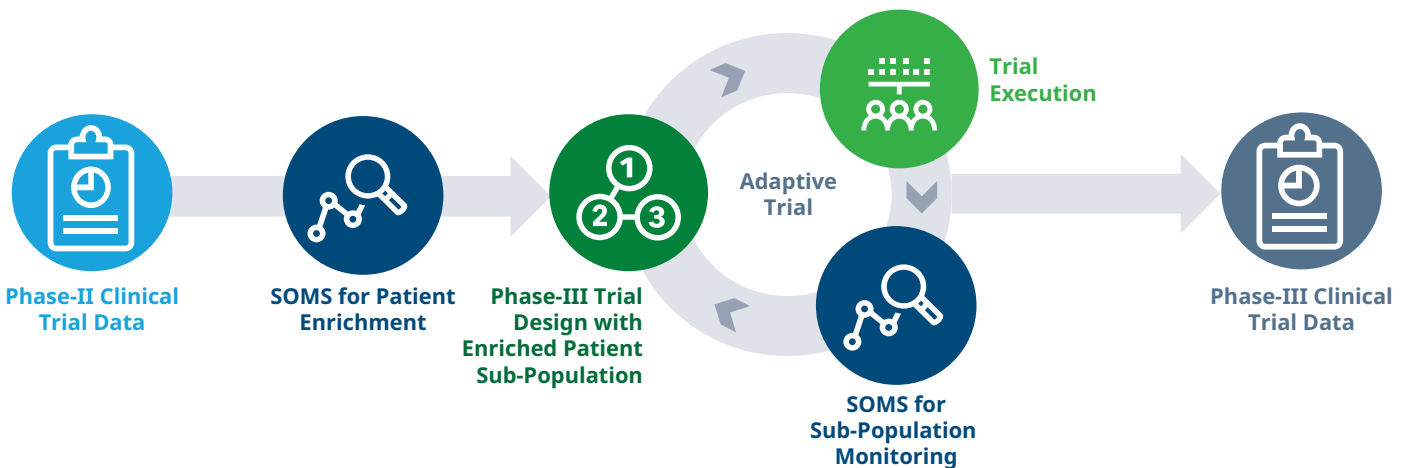
Sponsors often first leverage the SOMS platform at the end of phase 2 and during phase 3 trial planning. By reviewing phase 2 results with SOMS, they can proactively identify the sub-populations that are most likely to respond to the treatment, and determine which genetic, biologic, and/or environmental features define these populations.

The data will directly inform inclusion/exclusion criteria and primary and secondary endpoint selection and can potentially be used to reduce the required trial sample size by recruiting patients with strong treatment effect signals. All of these insights can help sponsors lower their costs while accelerating time to market for new drugs.

## Case study: Predictive data drives Phase 3 trial

IQVIA recently worked with a global pharma company that wanted to evaluate safety and efficacy of a new drug compared to the standard of care for a specific cancer treatment. Using the SIDES methodology, the platform identified six biomarkers in phase 2 data that were predictive of treatment effect, which they used to identify subgroups where the treatment effect was substantially different from the overall population. That analysis played a key role in the development of a tailoring strategy and the selection of the patient population for phase 3 trials.

### Utilize Machine Learning to Automate Sub-Population Identification





## MONITOR AND RESCUE TRIALS

Sponsors and investigators can continue to use SOMS applications throughout subsequent trials to conduct real-time patient monitoring. These ongoing analyses help them proactively identify the sub-populations who are showing the most promising response, and those who are not or who are at risk of adverse events. It can also help them uncover promising trends within a failing trial to support investment in further research. For example, if a small sub-population is responding well to a treatment where the majority are not, they can bring that trial to an end, and set up a new arm to support that specific target group.

In studies where trial results are inconsistent, SOMS analyses can support adaptive trial designs, where sponsors continually modify key components of the trial in response to the data collected. Data-driven adaptive trial designs ensure sponsors are focusing on those patients most likely to experience positive outcomes, which improves patient safety, reduces liability risks, and increases the likelihood of gathering positive outcomes data to support regulatory approval.

## VALIDATE INTERNAL STATISTICAL ANALYSIS

Many sponsors have in-house analysts who vet trial data to determine whether a trial is delivering promising results and should continue. While these analyses are a vital part of the drug development process, they can be unintentionally biased, particularly when a team or company is heavily invested in a trial's success.

Using impartial AI and machine learning driven analysis conducted through an SOMS platform, these analysts can more accurately determine whether their recommendations are overly optimistic. SOMS removes confirmation bias, improves objectivity and can yield more insightful results.

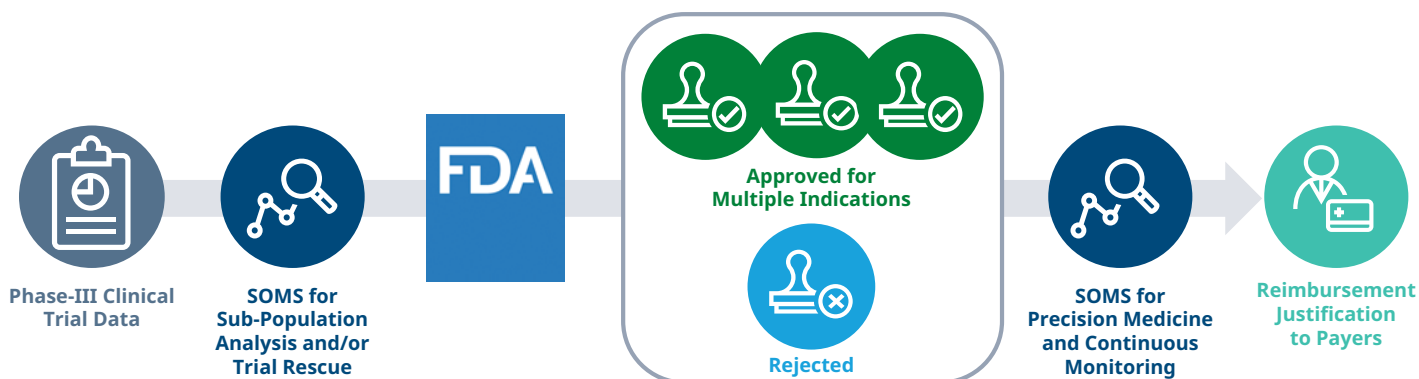
## Case study: Bacterial infections drug wins FDA approval

IQVIA worked with an emerging biopharma company that had two global phase 3 trials underway to evaluate the safety and efficacy of a new drug versus standard of care for treatment of bacterial infections. The original analysis demonstrated no overall treatment effect. However, an SOMS analysis retrospectively identified 26 biomarkers that were predictive of positive treatment effect. It also identified characteristics indicative of reduced treatment effect in the complement subgroup due to a safety concern that could be mitigated. Thanks in part to the analysis, FDA approved the new drug with a black box label for challenging cases when alternative treatments are not suitable.

## Case study: Not worth pursuing

IQVIA recently worked with a global pharma company that had phase 2b study results of a cancer treatment showing superior effect on overall survival for a specific subgroup. However, the phase 3 study yielded no meaningful results. Using the SOMS platform, we conducted a more detailed subgroup assessment, which found the data did not show consistent meaningful outcomes for any sub-population. As a result, the company abandoned further investment in the development of that asset.

## Utilize Machine Learning to Put Expensive Type 1 Errors Behind



### POST-APPROVAL APPLICATIONS

SOMS platforms can continue to offer benefits well beyond securing regulatory approval. The data and analysis they generate can help sponsors convince payers to support pricing decisions, and it can directly inform market planning and access, and sales strategies ensuring sponsors target the physicians and patients most likely to benefit from these treatments.

Sponsors can also use the data to support extension studies for new label claims, and to further hone populations based on data proving benefits and risks of adverse events.

### Case study: Identifying patients at-risk

IQVIA worked with a large pharma company that had two randomized open-label phase 3 programs for efficacy and safety evaluation of relapsed multiple myeloma patients. The sponsors wanted to understand if there were certain subgroups at increased risk of cardiac failure. SOMS was used retrospectively to identify subgroups at a higher risk compared to the overall population, using 25 biomarkers reflecting demographic and disease characteristics. The assessment uncovered two biomarkers that indicated potential risk factors.

The drug was later approved, and the analysis may have been used to address emerging safety concerns in ensuing studies.



## Part 3: SOMS — essential for targeted therapies

Gaining insights into which sub-populations are most likely to respond to a treatment is beneficial for any clinical research. But it can be a game changer for the development of targeted therapies and precision medicines. These therapies are designed to identify and destroy very specific proteins or molecular targets that allow diseased cells to grow and proliferate. The impact can be profound, but they only work in highly specific sub-populations based on a specific set of genes, biomarkers, disease stage, environment, or other treatment-relevant characteristics.

Dozens of targeted therapies have been approved primarily in oncology, and thousands more are in development, giving new life and hope to patients with diseases that were once considered terminal. However, the successful development of targeted therapies requires the ability to identify appropriate targets and track response in highly specific patient populations. These populations are often small, scattered, and difficult to identify, which can lead to high rates of exclusion during trial recruiting, and poor trial results if the trial design doesn't adequately identify the specific candidates likely to respond.

Consider chimeric antigen receptor T-cell (CAR-T) therapy, which is one of the most exciting developments in the oncology space. This targeted immunotherapy is driving durable responses in patients with previously unresponsive cancers. However, some patients in these trials don't respond at all, and a small but significant group experience rare but potentially fatal side effects, including cytokine-release syndrome (CRS), which leads to high fevers, joint pain, and a dramatic drop in blood pressure. Being able to proactively identify the patients who are responding from those who won't or who are at risk of CRS delivers significant safety benefits and improves the chances of delivering positive outcomes.

It also creates challenging cost-benefit scenarios for sponsors. These treatments have much smaller patient populations, which impact their revenue potential. Finding ways to reduce development costs and accelerate market access to take advantage of exclusivity are critical to delivering a value-driven treatment that benefits patients and sponsors. The SOMS platform delivers this added value potential by helping sponsors identify target populations faster and more accurately, and design trials that are more productive, cost-effective, and safer for the patients involved.



## Conclusion

One of the most effective ways to cut the cost of drug development is by reducing the rate of trial failure. SOMS platforms can provide the analytics and analysis necessary to achieve this goal, creating new commercial opportunities for sponsors, and bringing more lifesaving treatments to patients who need them.

# About the authors



**KAL CHAUDHURI, MBA**  
Principal, Sub-Population  
Optimization and Modeling Solutions,  
IQVIA

Mr. Chaudhuri leads the Sub-Population Optimization and Modeling Solutions product for IQVIA. His experience in new product development and global launch started with building shared and reusable medical imaging platforms and has continued through to the development of AI and machine learning based products and solutions for disease detection and personalized treatment through diverse delivery mechanisms.

Mr. Chaudhuri brings 25 years of experience leading technology and business change. He has worked extensively across technology enabled product life cycle management from organizational and process design, marketing and product management in healthcare and technology services through strategic partnership management and regulatory approval.

Prior to IQVIA, Mr. Chaudhuri led portfolio transformation for Ricoh and health imaging and cancer detection products for Siemens among other roles.

Mr. Chaudhuri earned an MBA from Columbia University in New York. He also is an alumnus of the Wharton School (University of Pennsylvania) and the Indian Statistical Institute.



**RUSSELL REEVE, PhD**  
Vice President, Decision Sciences,  
IQVIA

Dr. Reeve leads the Decision Sciences unit of IQVIA which provides customers with pharmacological and biostatistical expertise in study reporting, advanced analyses, and trial design. Working across the therapeutic spectrum, the team's recent experiences include vaccines, oncology, rheumatology, and rare diseases. Decision Sciences represents our clients at regulatory meetings, including both the FDA and EMA. Decision Sciences team members are active in research and thought leadership and are expected to publish in a peer-reviewed journal or contribute to a scientific book. We participate in many industry working groups and we host our own biostatistical conference.

Dr. Reeve's expertise is in vaccine development, nonclinical biostatistics (CMC), trial design — especially adaptive and personalized dosing designs — trial simulation, and biosimilars. Dr. Reeve has worked on development strategies for many vaccines (including influenza, HCV, and HPV), more than 50 biosimilar development strategies, has designed more than 50 trials per year, and has supported device submissions (including in vitro diagnostics such as ligand-binding assays).

Dr. Reeve earned a BS in Mathematics and Statistics from Utah State University, an MS in Operations Research from Rensselaer Polytechnic Institute, and a PhD in Statistics from Virginia Polytechnic Institute and State University.



**ADRIAN McKEMEY, PhD**  
Senior Vice President,  
Consulting Services, IQVIA



**PENNY RANDALL, MD, MBA**  
Vice President and Head,  
CNS Center of Excellence, IQVIA

Dr. McKemey is a founding member of the IQVIA Consulting Services team. As a Senior Vice President and Head of the R&D Strategy Solutions, Adrian focuses on business transformation, portfolio management, risk partnering, scenario planning and R&D strategies to help biotech, pharma and private equity develop next generation development and commercialization models.

Prior to assuming leadership at IQVIA Consulting Services, Dr. McKemey was a Principal with the Boston Consulting Group (BCG) working in the Life Sciences practice in New York helping pharma clients with business process reengineering and organizational change, along with new product R&D/Commercialization strategies. Dr. McKemey has also served as a pharmaceutical and diagnostic independent strategy consultant in London where he was a tenured faculty member at Brunel University and Menlo Park where he was a visiting professor at Stanford.

Dr. McKemey holds a PhD and BSc from University of London in High Energy Nuclear Particle Physics.

Dr. Penny Randall is Vice President and Head, CNS Center of Excellence at IQVIA. In this role, she is responsible for the enterprise-wide strategy for CNS, encompassing drug development and healthcare services. Dr. Randall has been involved in numerous successful drug development programs that have led to new treatments for patients.

Dr. Randall's scientific focus is on optimizing trial design and implementation to minimize the risk of inconclusive trials. She is also interested in leveraging disruptive technologies to modernize and accelerate clinical drug development, bringing new important therapies to the market more rapidly.

Board certified in psychiatry and addiction psychiatry, Dr. Randall completed her psychiatry residency at Georgetown University School of Medicine, and a research fellowship in anxiety disorders at Yale University School of Medicine. Dr. Randall received her medical degree from the University of Louisville School of Medicine and a graduate business degree from the University of California at Irvine, concentrating in healthcare management.

Dr. Randall has a background in academic psychiatry. She held faculty positions in the department of psychiatry at Yale and the University of California, Irvine.



**CONTACT US**

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