Modern clinical trials—apply a mix of co-innovation and best practices to improve productivity and drive ROI

Author:
John J. Doyle, DrPH, MPH, Chief Scientific Officer and President, Consulting Services, Fortrea

Acknowledgment:
The author would like to thank Fortrea colleagues Kenneth Park, MD, Georgina Strickland and Jeff Cohen for their input and involvement during the development of this article.

During each stage in the development of any medication, productivity is a crucial—yet elusive—measure of success. In broad terms, R&D productivity in drug development can be defined simply as the relationship between the value (both clinical and commercial) that is created by the new medicine and the investments that are required to create and commercialize that medicine (Box 1 & Figure 1).

Different levers are available to help pharma/life sciences stakeholders maximize productivity and improve their return on investment (ROI) throughout the entire drug-development lifecycle. Yet selecting the most appropriate levers to apply is a complex undertaking.

This paper is the first in a multi-part series that examines the range of options that are available to improve productivity throughout each stage of the clinical trial process. This series also provides recommendations for how to identify, prioritize and implement specific strategies that have the best chance of yielding the most immediate, demonstrable results.

There is no one-size-fits-all approach when it comes to improving productivity; rather, the opportunities will vary based on a wide range of factors discussed in this article and in the rest of this productivity series. To meaningfully streamline workflows and processes, optimize resource utilization and improve outcomes, pharma/life sciences stakeholders must critically rethink each step in the clinical trial process. Importantly, clinical trial sponsors and their clinical research organization (CRO) partners must break from the status quo and let go of the reflexive reliance on existing approaches and systems. The aphorism “nothing changes if nothing changes” applies here.

Instead, drug developers should strive to establish a rigorous, structured approach (with appropriate measurement throughout the process) to drive productivity gains.

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Productivity framework seeks to identify, assess and prioritize potential opportunities and to manage the implementation of the selected initiatives over time. It comes as no surprise to drug developers that trial costs continue to rise while productivity continues to lag (Figure 2). To drive the biggest productivity and ROI gains when time is constrained, drug sponsors and their CRO partners should strive to deploy parallel initiatives concurrently. Often, stakeholders focus on one initiative, roll it out as a pilot program, and assess broader implementation over time. Whether this is a strategic step-wise approach or a resource-constrained choice, the productivity impact will be limited.

A better approach is to run each initiative like a rigorous scientific experiment—monitoring and analyzing relevant metrics to develop data-driven insights that can be used to continuously refine the selected program improvements over time. Similarly, CROs must identify and deploy best practices that have emerged across many different trials. This will help to prioritize the options and ensure that each initiative is introduced at the optimal time and place in the trial process.

Such a rigorous approach will help to drive tangible improvements more quickly and enable head-to-head comparisons of parallel initiatives to be carried out, yielding insights that can inform continuous-improvement efforts.

Many specific options are available for trial sponsors and CROs to close productivity gaps and drive demonstrable ROI at every step of the trial process. For example, greater use of advanced modeling and data-analytics technologies—including those based on artificial intelligence (AI), machine learning (ML) and natural language processing (NLP) capabilities—can help to reduce timelines and cost while improving clinical and business outcomes and quality.

Similarly, the use of regulatory-grade real-world data (RWD) and real-world evidence (RWE) is playing a growing role in addressing the needs

Box 1

How do you define productivity?

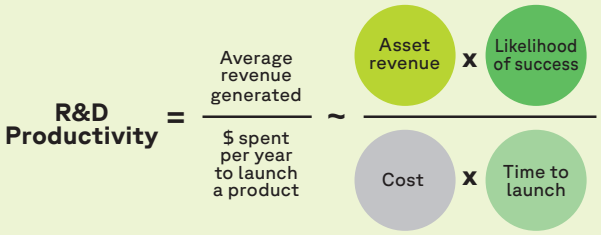
As a concept, productivity (as it relates to clinical trials) is a reflection of how much time, cost and effort it takes to bring a medication to market and how valuable that therapeutic intervention will be throughout its entire commercial lifecycle. Productivity can be measured in several ways.

- One approach is to assess productivity as the number of commercial assets in the portfolio, multiplied by the average lifetime revenue of each asset, divided by the cost of development per year for each asset
- An alternative approach is to assess productivity according to the average lifetime revenue per asset, divided by the average cost to bring that asset to market per year

Meanwhile, some stakeholders use the concept of effectiveness and efficiency as proxies for assessing productivity (these concepts are related but are not synonymous):

- **Effectiveness** refers to the extent to which the drug-development process is able to achieve its intended outcomes (to produce approved therapies that address unmet clinical need in patients)
- **Efficiency** refers to how well the resources (such as time, budget, personnel and more) are utilized to achieve the target outcomes of the drug-delivery process

Figure 1



Irrespective of how productivity is assessed, it is essentially a measure of the risk-adjusted net present value (NPV) of a particular pharma/life sciences asset.

of regulators, payers, prescribers and patients throughout the trial process. Increasingly, RWD and RWE provide data-driven insights related to patient populations, competitor therapies, clinical endpoints and more. Such insights can address sources of productivity losses that arise throughout the trial process—by informing protocol design and inclusion/exclusion criteria, improving patient recruitment and retention, reducing patient burden by enabling the use of external control arms and pragmatic/adaptive trial designs and so much more.

Table 1 reviews many of the common issues trial sponsors experience and shows some of the strategic levers that are available to enable specific productivity gains at various stages of the clinical trial process and drive ROI. These concepts will be discussed in greater detail throughout this multi-part series.

Importantly, implementing a comprehensive program to improve productivity requires a top-down commitment from management to ensure it is properly resourced. When drug developers are able to partner with a third-party CRO that has a deep bench of experience and expertise in clinical trial strategy, design and execution—and a fundamental commitment to driving productivity gains at every opportunity—such a partnership can streamline the execution of such a multi-faceted program. Co-innovation approaches can speed up innovation cycles, bring diversity of knowledge and insights to address complex challenges, and foster stronger ties between sponsor and CRO partner.

Any clinical trial represents a complex ecosystem of interconnected players. The role of the CRO is to integrate the elements seamlessly, bringing visibility and transparency into the entire trial process. Implementing strategic productivity improvements at each step delivers measurable results for the overall clinical and business outcomes. Such efforts also deliver stronger ROI for the drug developer.

As noted, this is the first paper in a multi-part series that will share actionable recommendations and discuss innovative opportunities for closing productivity gaps at specific points in the clinical trial process. The series will explore specific levers that can be considered—integrating such techniques as process redesign, strategic use of technology advances, modeling and simulation tools and other analytic best practices. It will also showcase several case examples to demonstrate the direct impact that measurable productivity gains have on overall clinical and commercial outcomes.

Factors undermining productivity objectives

Over the past decade, large and mid-size life sciences companies have been experiencing declining productivity. A variety of factors are driving this trend.

Consider some recent metrics that characterize the complex landscape today's drug developers face.

Figure 2

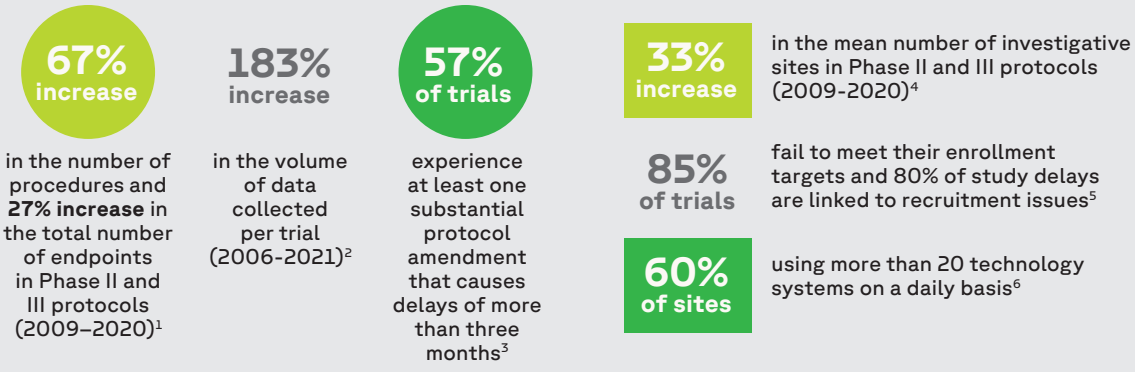


Table 1 *Strategic levers to increase productivity throughout clinical trials*

Operational challenge	Specific challenge	Use case examples	Metrics that demonstrate productivity gains
Regulatory and administrative complexity	Patient-focused drug development Diversity Action Planning (DAP) Endpoint optimization Protocol amendments Cycle time lag Trial monitoring Clinical Research Associate (CRA) management Study oversight Budgeting and contracting	Multi-stakeholder early engagement RWD-and AI-enabled DAP RWD-and AI-enabled protocol design Early engagement Product development team end-to-end engagement Real-time strategy efficiency-monitoring system Real-Time Scenario Intelligence Tool CRA app Study oversight hub Budgeting and contracting tool	Improved patient recruitment and retention Improved patient recruitment and retention according to diversity targets Reduced number of patients and data required Reduced protocol amendments and future study holds Reduced time lags between trial phases Improved CRA efficiency, site planning, trial management and reporting
Increasing competition for investigators and sites	Site-selection inefficiencies Investigator and site engagement Delayed site start-up Site network location and scale Site profiling	RWD- and AI-enabled feasibility analysis and site selection Expand assessment criteria based on data-driven patient-treatment patterns and site operations Site Advisory Board & Voice of Site Program Multi-tiered site relationships Site app Site training based on best practices Start-up hub and navigator to streamline site start-up Site-capability scan Country expansion into new markets Site profile and intelligence tool	Streamlined feasibility analysis Reduced pre-study visits Reduced data-mining cycle time Improved prediction of sites with better recruitment, reduced use of sites with poor recruitment record Improved recruitment, site engagement and overall site performance and communications related to KPIs Improved overall performance and data-driven next-best actions Improved site recruitment Increased patient retention Quality improvements Combined roles for site contracting and budgeting (to streamline enrollment and improve site experience) Accelerated equipment and inventory documentation Decreased recruitment costs (by using less competitive markets) Improved site feasibility assessment

Operational challenge	Specific challenge	Use case examples	Metrics that demonstrate productivity gains
Difficulty recruiting and retaining patients	Lagging patient engagement Reaching patients at home Precision medicine patient recruitment Adaptive trial design Patient pre-screening Multi-lingual consent	Voice of the Patient Patient experience data (PED) automated as output for all studies (to provide continuous protocol intelligence) RWD- and AI-enabled mobile patient engagement Patient app Fortrea's Patient Pre-Screening Tool Mobile study team to patients' homes Country-specific social media best practices and standards Trial-specific patient-engagement app Preferred precision medicine site and data partnerships Inclusion/exclusion criteria recommendations (both pre-and during trials) Site-based pre-screening tools for patients Automated consent-translation tool	Reduced development time by up to 50%, and budget by up to 30%, by developing and using a consistent set of patient-and site-specific templates Increased use of home services to increase patient retention Increased awareness, engagement and recruitment Increased recruitment and retention Decreased patient friction Decreased data gap Reduced overall costs
Monitoring inefficiencies	Site information exchange CRA inefficiencies Monitoring patients at home Quality management inefficiencies Site inventory management	AI-enabled site engagement portal and dashboard AI-enabled CRA visits and monitoring e-Consent electronic Clinical Outcomes Assessment (eCOA) Digital Health Technology (DHT) including sensors, wearables and virtual assistants Enhanced Risk-Based Quality Management (RBQM), oversight and central monitoring platform Inventory-management system	Reduced eligibility protocol deviations (up to 90%) Reduced CRA monitoring activity by using eConsent Reduced screening failure rate (by up to 40%) using offsite visits Reduced CRA travel and Source Data Verification (SDV) 40% data captured directly through sensors, eCOA (inc eDiaries + electronic Patient Reported Outcomes (ePRO)) = reduction in SDV and reduction in cycle time to lock Reduced Dropout rate by up to 15% through direct data capture Adding DHT reduced protocol deviations by up to 50%

Operational challenge	Specific challenge	Use case examples	Metrics that demonstrate productivity gains
Data management	Inefficient data-management review Serious adverse event reconciliation Local laboratory data review World Health Organization (WHO) drug coding Document capture Testing data	Device Master Record (DMR) automation Serious Adverse Events (SAE) Tool Local lab-automation tool WHO drug-automation tool Mobile document capture Test-data generation tool	0.25 Full-Time Equivalent (FTE)/month/study Increased overall efficiency
Biostatistics and statistical programming	Design speed and quality issues Standardization of tables, figures and listings	Clinical Metadata Repository (cMDR) Standard Tables, Listings and Figures (TFLs) and TFL Macros	Improved speed and consistency (through use of standard metadata)
Clinical and post-marketing safety	Answered Queries (AQs) Business partner submission compliance United Kingdom Medicines and Healthcare products Regulatory Agency (UK MHRA) acknowledgment rate Safety-data transfer	Process optimization for AQs Business partner submission tracking R2 XML Submissions Rave Safety Gateway Implementation	Reduced hold times and costs (by using centralized team) Improved monitoring and consistency Improved overall efficiency
Centralized delivery	Trip report review CRA preparation CRA dashboard	Trip Report Review (TRR) - eTMF Bot CRA Prep Pack Bot CRA Prep Pack Analytics Reporting Estimate (CARE) Dashboard	Improved efficiency Improved data monitoring, management and analysis

Driving ROI: Focus less on price increases and more on productivity improvements

Historically, many pharma/life sciences companies—large and small—relied heavily on steadily increasing drug prices and launching new indications as a key underpinning driving the ROI strategy for the drug portfolio. This is not a sustainable strategy for a variety of reasons, including the long-term impact of the U.S. Inflation Reduction Act (Figure 3).

By contrast, when drug developers and their CRO partners are engaged early in the planning process and focus on identifying and implementing parallel initiatives to close productivity gaps, they are able to improve overall ROI with reduced dependence on downstream price increases. In this way, improving productivity provides a direct opportunity to increase the clinical and commercial value of the therapy and help reduce overall risk.

For years, the prevailing rule-of-thumb has been that it takes more than a decade and an average R&D investment of $1 billion to develop and validate a promising investigational drug and bring an approved therapy to market. More recently, that benchmark has escalated.

The attrition-adjusted cost to develop a single novel asset is now estimated to be as high as $2.8 billion, according to a recent article from McKinsey Consulting.[7]

Meanwhile, the duration of many clinical trials continues to get longer. According to 2024 McKinsey analysis, between the periods 2011–2015 and 2016–2021, the average clinical trial lengthened from 41 months to 44 months for Phase III trials, and from 37 to 41 months for Phase II trials.

This increasing complexity provides strong head winds for trial sponsors and their CRO partners. Indeed, the complexity of clinical trials was cited as the number one issue impacting research sites in a 2024 survey by WCG.[8] With so many parallel drivers introducing uncertainty and complexity—including novel mechanisms of action (MOA), novel measures and assessments, site bottlenecks and other issues—it is more important than ever for drug sponsors and their CRO partners to work in close partnership.

The goal is to identify productivity lags that arise at every step in the trial process. The ability to implement specific initiatives that can streamline processes, shorten timelines, trim budgets and improve quality and outcomes provides direct impact on ROI. Thus such initiatives pay for themselves over time.

The cost structure of today's drug-development efforts is further impacted by the growing scientific complexity associated with so many of today's clinical trials. This is due in part to the growing proportion of today's drug pipeline that is devoted to biologics, cell-and-gene therapies, immunotherapies, orphan drugs for rare diseases and narrow oncology indications, and other complex specialty drugs. At the same time, high failure rates associated with many of today's innovative therapies reduces the overall yield—and thus ROI—of recent drug-discovery efforts. This makes it more important than ever to seek strategic productivity gains throughout the process to drive success and provide hedge against inevitable losses.

The U.S. Inflation Reduction Act (IRA) creates additional pressures

The 2022 passage of the U.S. Inflation Reduction Act (IRA) has the potential to further undermine ROI and net revenue and reshape priorities in the drug-development pipeline. While the full impact of the IRA will not be known for several years, the ability of the Center for Medicare and Medicaid (CMS) to negotiate price caps that will sharply curtail the revenue potential for certain medications (both small-molecule and biologic therapies) during the tail end of their commercial lifecycles. This is creating further uncertainty for many drug developers.

Considering that it takes several years for any drug to meaningfully recoup its R&D costs, and that drug prices typically grow by 5–10% year over year, the latter years in any drug's lifecycle typically represent the period of peak revenue. With the IRA's ability to curtail the time in the market at full price, drug developers must expand their arsenal of options for maximizing profitability by speeding the time to market, reducing overhead and development costs.

Figure 3

	Mean peak sales per approval ($US millions)	Total Global R&D Spend ($US billions)	Mean percent of total sales invested in R&D	Return on R&D investment
2005	$757	$94.2	18.2%	12-15%
2010	$816	$127.4	18.4%	9-11%
2020	$396	$159.4	20.9%	3-5%

Sources: Statista, Evaluate Pharma, Deloitte, Oliver Wyman

Meanwhile, price caps not only reduce short-term revenue, but by restricting cash flow today, such price caps are likely to force many drug developers to re-evaluate the focus and extent of their long-term clinical development efforts—which will directly impact patients and their healthcare providers.

In a related note, the IRA discourages pharmaceutical companies from researching additional indications for a drug by allowing the government to set a "maximum fair price" for a drug early in its lifecycle. This could have a chilling effect on innovation by financial incentives to conduct further research and clinical trials to explore expanded indications in reducing new patient populations once the initial price is set. Essentially, companies may be less likely to invest in post-approval research if they fear their potential profits from new indications will be capped by the government's price-negotiation process—even if those additional indications could significantly benefit patients.

Over time, the ripple effect of IRA-mandated price caps will also be felt worldwide for three reasons:

1. Global pharmaceutical producers are often heavily reliant on U.S. sales as part of their overall strategy
2. Drug pricing in many other countries is often indexed to pricing in the U.S.
3. The IRA may create additional headwinds on R&D innovation (given the uncertainty on long-term pricing and ROI)

Thus, the IRA is yet another factor that underscores the importance—and the urgency—of identifying and implementing a multi-faceted portfolio of initiatives that can improve overall productivity during each phase of pre-clinical R&D and the clinical trial process. When productivity improvements can reduce timelines and overall costs, drug developers are able to improve ROI in ways that don't depend as heavily on drug pricing as a primary way to maximize net revenue.

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Identifying specific opportunities to close productivity gaps

In general, the success of any specific drug-development effort is typically evaluated according to the following metrics:

- Increased revenue
- Increased speed
- Reduced costs
- Improved quality (which results when different types of failures are reduced throughout the trial process)
- Improved probability of clinical and commercial success

Targeted productivity-related initiatives—to be explored in depth in the next articles in this series—can help drive demonstrable gains in each of these objectives.

The most relevant objective(s) to focus on will vary from product to product and from company to company. And, while there will be baseline standard set for each objective, time and resource limitations underscore the need for drug developers and their CRO partners to prioritize where to lean in to create maximum impact.

The priority given to any one of the objectives noted above depends on many considerations—including the overarching clinical and commercial objectives for the therapy, the prevailing technical challenges, market opportunities, market obstacles, funding, both near-term and longer-term competitive strategies and more.

Similarly, depending on the size of the company, the product portfolio and the long-term business strategy, individual drug developers embrace the idea of productivity differently. For example:

- **For larger, established pharmaceutical/ life sciences companies** that already have a broad portfolio of products and a robust development pipeline, a primary strategic objective is often to maximize speed and success during the trial process, in order to optimize market access and market capitalization for the therapy in question
- **For smaller companies and startups,** a primary strategic objective is often to optimize the overall value of the investigational asset (or the overall company), whether their long-term strategy is to develop and commercialize the drug themselves, to partner with others, or to be an appealing candidate when seeking to be acquired by others

These factors create very different context and mindsets when it comes to prioritizing and implementing particular productivity-increasing opportunities. These drivers—and how different productivity levers can be applied to address these competing objectives—will be explored in depth later in this series.

It is worth noting that strategic efforts to ensure or improve quality throughout the clinical trial process are also critical for drug developers, trial investigators and patients. Quality by Design (QbD) principles can enhance productivity by ensuring that quality is built into the process from the beginning. Such efforts help to ensure better outcomes, improve data reliability and patient safety—and improve ROI by reducing costs and accelerating timelines.

Keep in mind that specific productivity initiatives that are aimed at increasing speed and shortening timelines, including cutting steps to streamline processes and reduce costs, can also lead to inadvertent tradeoffs in quality. Stakeholders must be aware of that risk as they are designing and implementing specific productivity-improving initiatives to ensure quality is improved, or at least maintained.

Pulling different levers at different phases of the trial process

The process of designing and executing clinical trials is an inherently complex undertaking. Nonetheless, a wide array of opportunities is available to drive productivity improvements at every step of the way. These include optimizng:

- **Protocol design** to reduce complexity, ensure the most appropriate endpoints are selected, improve statistical outcomes with rigorous scenario planning and ensure robust exploration of the pharmacokinetic-pharmacodynamic (PK-PD) relationship
- **Regulatory-submission strategy** to improve the likelihood of success
- **Data-collection requirements, procedures and systems** to reduce site and patient burden
- **Site-selection considerations** to ensure optimal site yield during patient-recruitment efforts
- **Patient-recruitment and enrollment strategy** to ensure the ideal number of eligible participants
- **Clinical trial operations** using the right mix of technology, data-driven strategy, best practices and domain expertise to improve operations and reduce site and patient burden
- **Data-science strategies and requirements** to enable the more clinically relevant insights
- **Safety, training and startup considerations** to streamline and safeguard operations and participants
- **Overall project management and communications** to improve overall quality and impact
- **Trial closeout** to enable earlier submission of trial data to regulatory authorities
- **White space between trials and phases** to shorten the overall clinical-development program timeline

In all cases, the ability to bring about tangible productivity improvements depends on involving the right industry subject matter experts and bringing to bear the right mix of state-of-the-technologies, best practices and strategic design overhauls to shorten timelines, trim expenditures and minimize the overall rates of risk and failure.

Subsequent articles in this multi-part thought leadership series will provide deeper discussion of the opportunities and obstacles associated with each of the specific levers that are available to improve productivity in each of these areas and will share case examples to illustrate the value of the approach.

Choosing the most relevant metrics to track success

When assessing competing options for improving productivity, stakeholders must conduct a thorough analysis to quantify the potential gains and assess the impact on ROI. In the absence of complete data—a common scenario—stakeholders are often left to make reasonable estimates and assumptions to predict how specific initiatives could impact the timeline and budget and improve speed to market and market growth.

Without perfect or complete data, drug developers and their CRO partners still have several options to gain insights that can inform next steps. For instance, they can compare their current performance and approaches against the industry-accepted benchmarks and work closely with CROs, technology vendors and trial sites to provide input versus best practices. Benchmarking industry best practices will help stakeholders to prioritize problems and productivity-enhancing options. Such efforts are more productive when the members of the ecosystem are encouraged to collaborate closely, share knowledge and experience and innovate fearlessly together.

Meanwhile, without complete data, stakeholders can still make reasonable projections of the potential gains associated with any productivity-improving initiative, as well. By creating an estimate of the value of the potential gain and then pairing that estimate with industry-accepted standards, stakeholders are able to quantify the potential impact in terms of reduced budget, shortened timelines, reduced failure rates, improved patient recruitment, reduced protocol amendments and more.

It is critical to remember that any metrics are only valuable when they are tracked and acted upon. The success of any new initiative is not judged on the basis of its launch—but on its final performance. By continuing to measure the impact of new activities, processes can be refined and adjusted to maximize impact and achieve the desired outcomes.

At the end of the day, the goal for drug developers and their CRO partner is to identify and implement a portfolio of productivity-enhancing initiatives that convert innovation into value, so that promising investigational therapy breakthroughs can reach patients and providers more quickly, pharma/life sciences innovation can flourish and drug-development pipelines can remain robust. Those who fail to tackle this challenge head-on and investigate the opportunities available may soon be left behind.

John Doyle, DrPH, Chief Scientific Officer and President of Consulting Services at Fortrea.

John joined Fortrea in October 2023 and leads a global team of expert consultants across the product development lifecycle, helping customers navigate complex and fast-changing business and regulatory environments – driving productivity and innovation strategies to accelerate drug development that leverage data, technology and advanced analytics. The team's solutions include clinical development and regulatory strategy, real-world evidence, market access, health economics and outcomes research (HEOR), medical writing and publishing, as well as specialist services, such as pediatric plan development, diversity action planning and orphan drug designation.

John received his Doctorate and Master of Public Health degrees in Epidemiology from Columbia University, and BSc. in Business Management & Applied Economics from Cornell University. Dr. Doyle maintains a faculty position in the Department of Epidemiology at Columbia University.

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