A Science-Based Rationale for Abandoning Obsolete Standard-of-Care Cancer Treatment Dogma in favor of

Precision Medicine's More Conservative Approach

Part 1: Why and How Payers Must Serve as Catalysts for Change

A Series of Special Reports from the

TPA Network Research Consortium
a Healthcare-Focused Non-Profit Enterprise

Abstract / Executive Summary

Genomics as the Foundation of Precision Medicine

The integration of modern genomics into cancer care has profoundly enhanced our understanding of the disease and revolutionized our ability to treat it. The foundation of precision medicine, genomics enables the selection of targeted and effective therapies based on each patient's unique molecular profile. This approach marks a significant departure from traditional one-size-fits-all standard-of-care (SoC) therapies.

A More Evidence-Aligned Approach to Cancer Treatment

Precision medicine is a conservative, evidence-based upgrade to SoC treatment. Identifying biologically matched drugs eliminates ineffective treatments, reduces toxicity and improves outcomes. By contrast, SoC cancer regimens often waste resources on low-clinical-value treatments that ignore tumor variation.

Despite these advantages, payers have been slow to adopt genomics-driven precision medicine. This hesitation reflects limited awareness, persistent misconceptions, and insufficient or unclear guidance on implementation. Consequently, many payers continue to rely on the stale, pre-genomic era SoC approach to cancer treatment, missing opportunities to improve patient outcomes and contain healthcare costs.

A Framework for Payer Action

Our unbiased research and analysis helps healthcare providers evaluate new medical technologies, plan participants obtain leading-edge care, scientists advance medical research, and payers reduce risk.

This first-in-a-series of payer-focused reports provides a forthright perspective on the current state of cancer care and explains how precision medicine improves outcomes, enhances quality of life and contains cost. To assist payers, the *Research Consortium* created a *Precision Medicine Protocol* to serve as a practical framework for driving change. This piece describes how payers can improve survival and contain costs by prioritizing genomic diagnostics, aligning coverage with biologic rationale, and shifting reimbursement toward value-based models. By funding targeted testing, supporting molecular decision-making infrastructure, and discouraging empiric therapies with poor expected benefit, payers can reduce avoidable utilization, prevent futile care, and enable more durable, personalized treatment strategies. This approach is conservative with waste, not with ambition … and it allows payers to pursue improved survival and enhanced quality of life while containing the total cost of care.

Computers and Cancer: Technology Adoption Déjà Vu

Early on, *computers* were thought of as integrated systems rather than as flexible combinations of hardware, software and applications. Back then, computers served specialized fields (e.g., science, industry, business) and manufacturers targeted specific markets. Indeed, it would have been almost blasphemous to suggest that a *scientific* computer could be used to automate basic accounting functions.

Today, much of *cancer care* remains rooted in outdated approaches, particularly the standard-of-care (SoC) practice of defining cancer types based on the affected organ, rather than the genomic drivers behind each patient's unique cancer. This results in SoC treatments that are limited to organ-specific drugs, ignoring genomic similarities across cancer types, e.g., drugs that are effective against a genomic marker in breast cancer may not be considered when that same driver appears in liver cancer. This logic mirrors our early flawed thinking about computer specialization, *with more profound consequences*.

Genomics: Unlocking the Potential of Anti-Cancer Treatment

No two cancers are alike. As world-renowned oncologist and cancer researcher *Dr. Razelle Kurzrock* identified more than a decade ago, *cancers are like snowflakes*: they share similarities, but no two are exactly alike. Indeed, even within an individual, there are differences in the genomics of each tumor. A pioneer in applying genomics to cancer treatment 15+ years ago, she leveraged genomic information to increase the effectiveness of cancer drugs that had demonstrated very low success rates because, as she notes, *"It doesn't matter how good the drugs are, if you give them to the wrong patient, it's not going to work."* This captures the fundamental shortfall of SoC cancer treatment and the reason why we must move beyond the *cancer industrial complex*'s outdated population- and sameness-based SoC approach to care that results in one-size-fits-all, one-drug-at-a-time therapy that often results in unremarkable outcomes.

Many other traditional SoC approaches, methods and tools used to treat cancer fail on a number of levels:

- *Biologic heterogeneity (variation)*: SoC cancer treatment regimens (e.g., "every patient with stage or characteristic X is treated with regimen Y") ignore that two tumors with the same histology (i.e., anatomical observations visible with a microscope) can have entirely different molecular drivers.
- *Toxicity and benefit mismatch*: Empiric therapy is medical treatment based on experience or a clinical "educated guess" in the absence of complete or perfect information. In SoC cancer care, this can lead to the use of empiric chemotherapy — *often administered before the confirmation of a definitive cancer diagnosis* — that delivers modest benefit at high toxicity and cost.

For patients, physicians and payers alike, the solution is a move to *precision medicine*, a comprehensive patient-centric approach to care that recognizes the critical impact of each cancer's molecular profile. Precision medicine uses genomic information about a cancer's unique molecular makeup to inform and guide science-based treatment decisions, e.g., making a diagnosis, creating a customized patient-specific treatment plan, monitoring disease progression, measuring treatment efficacy. As the precision medicine approach is fundamentally different than traditional SoC medicine, the transition to it will be profound.

Evidence that individualized cancer therapy can outperform SoC treatment abounds. Numerous clinical trials and real world studies of matched, multi-drug regimens show that higher "matching scores" between tumor alterations and chosen drugs correlate with improved response rates, progression free survival, lower severe toxicity and sometimes overall survival vs. the SoC approach. When therapies are selected based on tumor biology, you can sometimes use fewer or lower intensity agents with better benefit–risk balance — more conservative in terms of unnecessary treatment, not in terms of ambition for outcomes.

The challenge for oncologists is that there are 300+ FDA-approved cancer drugs, many that are used in combination. They generate 4.5+ million one-, two-, and three-drug treatment options — far more than any individual can evaluate and assess. To identify the best treatment, oncologists must determine the unique genomic drivers of each patient's cancer then match those drivers with the drugs most effective at targeting the specific gene mutations fueling the cancer's growth. This is no small task—until recently.

The case study below, from a *2022 Research Consortium paper*, illustrates how dramatically a patient's options can vary when treatment selection is guided by genomic information vs. organ site alone.

Standard-of-Care Treatment Options

SoC cancer treatment is often one-size-fits-all, one-drug-at-a-time care. Consequently, comprehensive molecular testing (e.g., DNA and RNA analysis) to identify the genomic drivers of each patient's unique cancer is not routinely performed. Genomic tests were ordered for this (gastrointestinal carcinoma) patient as he was in a clinical trial. The result: *nine actionable genomic markers were found to drive his cancer.*

Confined only to organ-related treatments, there are just three FDA-approved drugs for this cancer type, each to be used separately. Sadly, they target only three of this cancer's drivers, *leaving six untreated*.

Comparative Predictive Effeciveness Results

	SCORE	Recommended Treatment Options		
		Drug 1	Drug 2	Drug 3
3- Drugs	83%	**Cisplatin**	**Palbociclib**	**Bevacizumab**
	83%	Carboplatin	*Palbociclib*	*Bevacizumab*
	78%	Olaparib	*Palbociclib*	*Sorafenib*
2- Drugs	58%	Carboplatin	*Bevacizumab*	Off-Label Combination of 3 Approved Drugs
	58%	*Olaparib*	*Bevacizumab*	
	53%	Cisplatin	*Sorafenib*	
1- Drug	33%	Carboplatin		
	33%	Olaparib		
	15%	*Sorafenib*		

Each of these Approved On-Label Medications, are Popular, Comparatively Low-Value, Options

Approved drugs, used in an off-label combination for this indication, are in *italics*

Precision Medicine Treatment Options

Precision medicine is an approach to treatment that recognizes the critical impact of each cancer's unique molecular profile and uses genomic data to inform and guide science-based treatment decisions.

When treatment selection is guided by genomic information rather than organ site alone, the number of evidence-informed options expands exponentially. For this patient, genomic analysis identified 23 FDA-approved cancer drugs that matched at least one of the cancer's nine drivers, increasing the available treatment options from three to 2,024. An AI-enabled treatment-matching tool then scored and ranked these options to highlight the most effective ones. The two highest-ranked treatments targeted 83% of this cancer's drivers, compared with just 33% targeted by standard-of-care therapies.

Although the effectiveness of molecularly targeted multidrug treatments for advanced cancer is well established, few oncologists are familiar with the cost of the cancer drugs they prescribe, or which will be more cost-effective, deliver a better return-on-investment or represent a financial value. One reason is that, unlike most countries, the United States does not employ *comparative effectiveness research* to evaluate how well drugs perform relative to one another. In addition, more than 70% of physicians are unaware that the FDA does not require the manufacturers of new drugs to demonstrate that they are better than existing therapies as it does not approve drugs based on clinically meaningful benefits. Further, many physicians mistakenly believe that breakthrough therapies (most of which are for cancer treatment) are subject even greater scrutiny. Lastly, although it may be intuitive to believe that a combination of multiple high-cost drugs would be more expensive than using a single-drug or another standard therapy, a 2022 *Research Consortium* study shows that this is not always the case. Together, these misconceptions about the actual efficacy, cost and value of cancer drugs can lead physicians to overprescribe them.

The lesson from *computers* is clear: *technology classifications that once seemed fixed can become barriers to progress when their original classification is let to determine their potential uses*. Those who govern our healthcare system risk making the same mistake in *cancer care* if they continue to allow organ-defined therapy categories to override evidence-guided, genomic-informed decision-making.

Organ-based cancer treatment must be superseded, as it excuses decision-making based on incomplete knowledge. Ironically, by contrast, precision medicine's science-based, *look-before-you-leap* treatment approach is a *more conservative* course of action vs. blindly following obsolete pre-genomic era dogma. It is high time for payer and physician leaders to *earnestly* embrace precision medicine. To do otherwise would be to support more wasteful spending on high-cost, low-clinical-value drugs … and continue to deny patients access to vital genomic testing and the option to try potentially viable FDA-approved cancer drugs.

Standard-of-Care to Precision Medicine Transition Challenges

We have studied genomic-informed cancer care for several years and observed that some 80% of cancer patients receive sub-optimal care. The contributing factors are numerous and varied and include these:

Patient Challenges

- Insufficient patient education and empowerment, leading to little shared decision-making.
- Second opinion anxiety, discouraging the development of interdisciplinary care teams.

PCP/Oncologist Challenges

- Low functional knowledge of genomics, cancer biology, molecular medicine, etc.
- Scant familiarity with precision medicine approaches to cancer diagnosis and treatment.
- Inadequate understanding of why, how, and when to use comprehensive molecular profiling.
- Hesitancy about interpreting / acting on genomic data due to concerns re: clinical competency.
- High cancer misdiagnosis rates resulting from incomplete knowledge of disease assessment.
- Inadequate real-world experience employing genomic information re: treatment selection.
- Limited access to AI-enabled, genomic-powered treatment decision-support tools.
- Virtually no pre-treatment efficacy testing or post-treatment efficacy assessment.

Health System Challenges

- Deficient EMR systems and the lack of a current, real-time longitudinal health record.
- Very limited employment of technology-enabling platforms to enable care team collaboration.
- Insufficient access to convenient cancer-care patient advocacy and navigation resources.
- Poor care, and gaps in care, resulting from repeated avoidable medical care delivery errors.
- Insufficient collaboration between academic and community-based oncologists.
- Avoidable wasteful spending and resource depletion due to administration bureaucracy.

Cancer Industrial Complex Challenges

- Shortage of medical schools, oncologists, cancer care clinicians and nurses.
- Scarcity of advanced degree programs focused on precision medicine.
- Insufficient training in genomics, cancer biology, molecular medicine and AI-technology.
- Continued reliance on the outdated organ-based paradigm for cancer diagnosis and treatment.
- Barriers to the adoption of novel combinations of FDA-approved anti-cancer therapies.
- Issues with FDA new drug approvals, especially fast-tracked "blockbuster" drugs.
- PBM interference with free-market access to fairly priced anti-cancer therapies.

Payer/Plan Sponsor/TPA Challenges

- Few focused, dedicated programs or policies to control cancer risk and care.
- Poor benefits design that contributes to inefficient, more costly care and poor outcomes.
- Limited awareness among medical directors of the efficacy of precision medicine vs. SoC.
- Misconceptions about precision medicine and the true cost of not adopting it.
- Clinical utility measures that focus primarily on provider value rather than patient value.

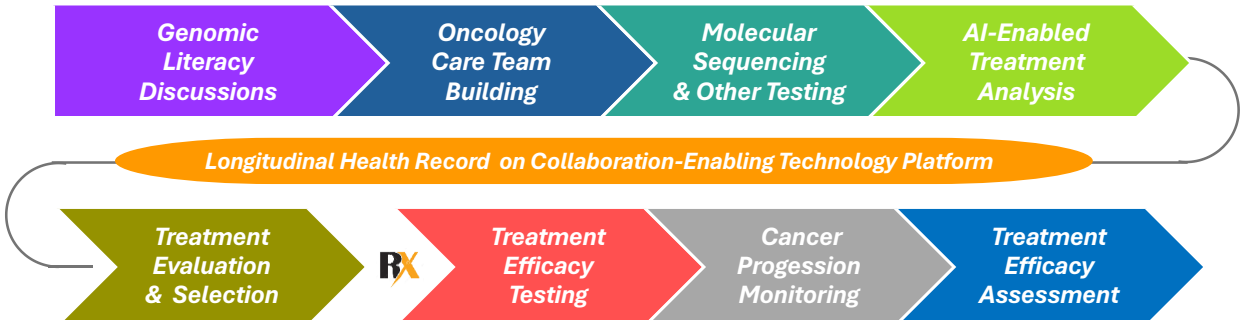
As it takes 15+ years on average for a new medical technology or healthcare innovation to get into wide-spread clinical use, these problems will not be resolved soon. This is largely because payers still use narrow, outdated *clinical utility* definitions, and medical guideline creators employ consensus decision-making that inherently leads to watered-down, lowest-common-denominator policy.

There are however, strategies, initiatives and tactics that payers, administrators, ESL carriers and medical management companies can pursue in the interim to mitigate the adverse impact of these challenges on their plans and on participants with cancer. The approach begins with our precision medicine protocol.

A Precision Medicine Cancer Care Protocol

A healthcare protocol is a clearly defined, standardized, evidence-based set of guidelines that informs clinical decision-making. It provides care teams with a consistent framework for navigating complex care environments while minimizing errors and variability in care. As a trusted foundation for care delivery, a healthcare protocol helps ensure that care is safe, coordinated, effective, and high quality across all clinical settings, regardless of the provider. Healthcare protocols support adherence to best practices and current evidence-based research while preserving the role of professional judgment.

To address the challenges that impede the effective, efficient, and empathetic delivery of high-quality personalized cancer care, the *Research Consortium* created a data-driven *precision medicine protocol*. Patented on the *patient active* concept created by cancer advocacy pioneer *Dr. Harold Benjamin*, the protocol catalyzes patients from passive bystanders into informed, engaged, and empowered shared decision-makers. It also leverages the approaches, tools, and technologies available to oncologists today.



As illustrated above, it consists of a series of well-defined steps which, when followed, have proven to be effective at shepherding patients through the cancer journey by

- educating patients about cancer, genomics and available treatment approaches,
- empowering patients to be active informed participants in shared decision-making,
- developing a multidisciplinary care team comprised of academic and non-academic clinicians,
- clarifying care team member roles and responsibilities to improve clinical workflows,
- facilitating real-time care team collaboration on a dedicated cancer care platform,
- creating a single-source, current, real-time online longitudinal health record,
- performing comprehensive molecular testing to identify the cancer's drivers,
- employing AI-enabled technologies to identify the most effective treatment options,
- using advance molecular analysis to predict the efficacy of the proposed therapy,
- performing pharmacogenomic testing to inform treatment dosing and potential interactions,
- conducting periodic genomic testing to monitor disease progression / therapy effectiveness, and
- tracking treatment response, managing side effects and adjusting as needed.

Following this protocol cannot guarantee better outcomes, however it will likely result in

- better, more efficient and more collaborative physician management of patient care,
- increased patient and physician confidence in the proposed treatment's efficacy, leading to greater patient risk-taking, a wider range of outcomes and better prospects of success,
- minimizing patient treatment toxicity and reducing therapy abandonment,
- speeding time-to-diagnosis and time-to-care while reducing disease progression,
- lessening patient and clinician anxiety with the identification and evaluation of all care options,
- support for patients navigating our fragmented, procedure-laden healthcare system,
- reducing wasteful spending on high-cost, low-clinical-value drugs,
- standardized and consistent metrics for biomarker-based treatments,
- eliminating patient "financial toxicity" and the risk of medical-related bankruptcy, and
- improving patient health outcomes and quality of life.

What Payers Can Do to Drive Change in Cancer Care

Payers seeking greater control over the delivery, quality and cost of cancer treatment must acknowledge the limitations of the current standard-of-care approach to cancer care and facilitate access to precision medicine, rather than maintaining barriers to it. This requires giving patients, caregivers and clinicians the policies, tools and resources needed to correctly diagnose and treat the disease in an efficient, effective, empathetic and cost sensitive way. The following steps outline how payers can drive this change:

Our experience is that cancer patients and their oncologists rarely alter their routines unless change is required. To transition away from SoC cancer treatment to precision medicine, payers must serve as the catalyst for change. They can do this by establishing dedicated initiatives; and modifying their benefit plans, administrative processes and medical management provisions, policies and practices. With this responsibility in mind, payers must take these deliberate steps to advance precision medicine adoption:

Build Precision Medicine Expertise

- Engage an oncologist advisor with experience and expertise in precision medicine.
- Develop a sufficient understanding of precision medicine to evaluate and endorse its use.
- Address misconceptions about the cost of precision medicine compared with SoC treatment.
- Broaden the clinical utility construct to include patient-focused measures of value.

Enable Precision Medicine Delivery

- Create a comprehensive, dedicated cancer care program and / or benefit.
- Employ an AI-enabled interoperable technology platform to facilitate care team collaboration.
- Provide access to patient advocacy and cancer care navigation services.
- Require cancer patients to undergo pharmacogenomic and comprehensive molecular testing,
- Deny authorization of treatment plans that lack a solid genomic rationale.
- Contract with, and steer patients to, value-based cancer centers of excellence.
- Exclude obtaining care from oncology practices that are owned in part by drug distributors.
- Carve out specialty drugs prescribed to treat cancer from the PBM contract.
- Require disease progression monitoring and treatment efficacy measurement.
- Negotiate a premium discount from stop-loss carriers for investing in precision medicine.

Although payers may be hesitant to require cancer patients to follow a specific protocol as a condition of coverage (e.g., requiring genomic testing), the increasing adoption of precision medicine and its likely emergence as the standard of care creates avoidable legal liability for payers. Consider the following:

- Plaintiff attorneys representing plan participants having cancer may contend that an ERISA plan's denial of coverage for comprehensive molecular testing constitutes a failure to fulfill the plan's fiduciary responsibility to provide participants with access to legitimate medically necessary care.
- Allowing a cancer patient to receive high-cost treatment, when comprehensive molecular testing could determine in advance that the treatment would provide no clinical value, may constitute the avoidable waste of plan assets and patient funds on treatments void of a solid genomic rationale.
- Similarly, failing to require comprehensive molecular testing to validate treatment selection could be viewed as enabling the use of an ineffective or low-clinical-value treatment, subjecting the patient to undue toxicity and unnecessarily delaying the selection of an effective treatment.

Alternatively, payers can proactively employ precision medicine to support and strengthen coverage and authorization decisions, e.g., specialty drug authorizations. By grounding these decisions in scientific evidence and patient-specific genomic information, payers can validate coverage and authorization determinations while promoting the standard, consistent application of care and authorization policy.

Final Thoughts / Call-to-Action

Cancer treatment decisions depend on many factors, including tumor biology, disease stage, molecular features, social determinants of health and the patient's overall health and preferences. AI-enabled, genomic-powered precision medicine can help align treatment with these patient-specific considerations by supporting less risky, science-based, and personalized care. By identifying treatments that are more closely matched to the characteristics of an individual's cancer, this approach offers a greater probability of treatment success and may provide greater financial value than standard-of-care treatment.

Comprehensive healthcare coverage is a cornerstone of equitable and effective cancer care. Coverage decisions shape access, quality, cost and outcomes across the cancer journey, influencing everything from treatment initiation to long-term survivorship. Decisions that deny, delay, or disrupt coverage affect both the care patients receive and the outcomes they experience. Because payers make coverage decisions, ***the burden is, in great part, on payers to drive the change to precision medicine for cancer patients.*** That responsibility cannot rest entirely with providers and health systems, which do not control coverage determinations. By supporting precision medicine, payers promote more effective, individualized cancer care while addressing the quality, cost and value considerations attendant to coverage decisions.

In later installments of this series, we provide greater detail about our precision medicine protocol; challenge conventional thinking about combination drug treatments and their cost and value; and show payers how to use value-based purchasing to gain greater control over oncology specialty-drug spending.

An abstract / summary of this document is available online to read or download here.

About the Author

Richard Nicholas is a seasoned industry veteran having nearly five decades of executive experience in various healthcare sectors. He has owned and held senior leadership positions with national third party administrators and managed care organizations and created one of the first HMOs in Mexico. For years, he facilitated TPA mergers and acquisitions for many of the nation's leading insurers and TPAs.

Mr. Nicholas has lectured extensively, both domestically and abroad, on topics of interest to many healthcare stakeholders, including at annual meetings of the *National Association of Health Underwriters*, the *Society of Professional Benefits Administrators*, the Mexican Social Security Institute (IMMS) and the *Mexican Foundation for Health*. He testified on regulatory matters at hearings before the *U. S House of Representatives Ways & Means Committee* where he represented the plan sponsors of some 200 TPAs.

Richard has authored articles for, and been quoted in, many publications including *The Wall Street Journal, USA Today, HR Horizons* and *Mexico Business*. He wrote of one of the earliest books on corporate healthcare cost management and authored many white papers, reports and scholarly presentations that have provided authoritative guidance on topics of interest to payers, providers and plan participants.

At the behest of other industry veterans, Richard created the TPA NETWORK *Research Consortium*, a non-profit, industry-wide healthcare research initiative that helps providers evaluate and assess new medical technologies, plan participants obtain leading-edge healthcare, scientists advance medical research, and payers reduce their risk … by conducting payer-focused translational research, in real-world settings. Richard holds a BA *with distinction* from *Boston College* and an MBA from the *Duke Business School*.

Funding Statement If you find value in this type of unbiased, payer-focused research and analysis, please consider supporting the TPA Network *Research Consortium* by making a tax-deductible contribution to our non-profit initiative or engaging us to perform an educational, consultative or advisory assignment on this or another topic.