# Investigating Factors Behind Uptake of Precision Medicine Practices in Oncology

A Research Paper submitted to the Department of Engineering and Society

Presented to the Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science, School of Engineering

**Katherine Anne Goundry**

Spring 2024

On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Advisor
Caitlin D. Wylie, Department of Engineering and Society

## Introduction

Precision medicine has emerged as a forefront approach in cancer research and treatment, focusing on evaluating biomarkers within patients to tailor therapies for improved outcomes. In oncology, the precision medicine approach to cancer therapy begins by evaluating relevant biomarkers within the patient, such as proteins, RNA and DNA transcripts, or mutations. The results of these tests are then compared against other patients and are used to predict whether a patient will respond to the therapy of interest. This allows the clinician and patient to select therapies that are more likely to succeed, reducing the need for trial and error of different treatment options and providing timelier treatment to the patient. Ultimately, this approach improves overall survival rates and quality of life (Ashley, 2016). As the precision medicine framework is introduced to new immunotherapy and chemotherapy drugs being brought to market, it is imperative that they are made available to patients as quickly as possible to maximize the number of patients who may benefit from precision medicine in the future. Currently, among the eligible cancer patients who can receive genetic testing to inform their chemotherapy treatment, only a limited set of patients goes all the way through the process and receives treatment based on the results of appropriate biomarker testing. For example, in non-small cell lung cancer (NSCLC) patients alone, on average 49.7% of the 500,000 patients eligible for genetically informed testing did not receive the correct treatment due to delayed and uneven implementation of new practices in the United States (Sadik et al., 2022). This decreases the number of patients who receive the treatment plan recommended by national boards and reduces their survival rates and quality of life. This phenomenon precludes a wide range of eligible patients from treatment across numerous malignancies that have received precision medicine treatment. To improve this process, we must first understand the current implementation process. To that end, I examined in depth the past integrations of precision medicine into the clinic.

The use of genetic testing to select patients to receive specific types of chemotherapy is the premier form of precision medicine that has been developed and integrated into the clinic within the last two decades. Its implementation differs significantly from the introduction of new drugs due to its complexity. Genetic testing to inform chemotherapy treatment requires (1) initial clinical evaluation and biopsy referral, (2) biopsy collection, (3) biomarker analysis, and (4) test

result reporting and a clinical treatment decision (Sadik et al., 2022). Implementation challenges arise from various factors at both the organizational and practitioner levels at each stage of this process. Consequently, integrating genetic testing into clinical practice presents distinct challenges that require a unique uptake process compared to other clinical advancements.

It is commonly thought that once successful therapies and advancements are discovered, they are immediately celebrated and used in the clinic because of their proven life-saving benefits. However, the process of adopting new advancements, especially in medicine, requires a lengthy implementation process so complex that a discipline, implementation science, has been created to investigate it. Implementation science is dedicated to investigating how evidence-based practices and new research progress from discovery to benefiting patients and society. The science examines factors related to the adoption of new practices, particularly barriers to beneficial practices. In medicine and cancer research, this process includes (1) basic research discoveries, (2) technology development, (3) testing and clinical trials, (4) commercialization, (5) regulatory approval, and (6) voluntary adoption by authorized technology users and healthcare providers (Bauer & Kirchner, 2020). Despite their vast benefits, the adoption of new technologies into practice occurs over an extended period, and in biomedical innovation, physicians tend to adopt these solutions months to years after their commercialization.

I intend to investigate the factors contributing to this delay, aiming to address them in future implementations of precision medicine. My goal is to identify key areas for focus for groups developing and commercializing new precision medicine techniques, with the aim of increasing the number of patients receiving state-of-the-art treatment.

The implementation of precision medicine techniques in oncological practices follows the pattern of adoption defined by the theory of diffusion of innovations. This theory describes how new advancements spread through society over time and categorizes individuals by their speed of uptake (Rogers et al., 2008). The factors contributing to this pattern fall into the categories outlined in Pacey's triangle, which characterizes them as cultural, institutional, or technological (Pacey, 1985). These factors together determine the pace of implementation in precision medicine in chemotherapy practices. Understanding these elements will lead to improvements in the effective and efficient introduction of new medicine.

## Physician Level Factors

The process of integrating new innovations into clinical practice requires not only technological advancements and commercialization but also a conducive environment for acceptance. Pacey's Triangle postulates that advancements succeed when their organizational, technical, and cultural elements align (Pacey, 1985). Precision medicine exemplifies this theory, as these three elements not only affect its implementation but also dictate the pace of adoption by clinicians. The cultural aspects surrounding precision medicine are influenced by the environment and relationships that oncologists work in, which is evident in their attitudes toward its rise.

Physicians bear significant responsibility for adopting new practices and clinical recommendations to improve patient care. However, almost all advancements in medicine carry costs in addition to benefits, necessitating careful consideration by physicians before implementing new practices to protect patients. Physicians must understand the empirical evidence surrounding the advancement, the nuance of recommendations made by their governing bodies, and other considerations that are specific to individual patient's needs. This complexity increases the difficulty of adopting new practices and slows the pace of implementation.

Physician attitudes toward precision medicine reveal several factors that impede the adoption of new practices. These attitudes correlate with openness to using new precision medicine practices; those with more positive attitudes express fewer concerns (Vetsch et al., 2019). However, some physicians remain hesitant to include precision medicine in their practice due to a lack of robust studies and considerations of financial and time costs (Gingras et al., 2016). Physicians also cite a lack of confidence in their own knowledge and understanding of genetic testing and precision medicine practices, preferring to rely on genetic counselors for guidance (Vetsch et al., 2019). This complexity reduces the proportion of patients who benefit from precision medicine (Sadik et al., 2022). "Oncologists' even express hesitation in complying with recommendations from federal governing bodies such as the National Comprehensive Cancer Network (NCCN) and National Cancer Institute (NCI). This hesitation is due to the complexity of evidence from clinical trials, including biomarkers and other evidence (Erdmann et al., 2021).To address physicians' hesitancy toward adopting precision medicine practices, such as lack of confidence, financial concerns, and complexity of evidence, comprehensive continuing

education programs as well as robust, well distributed research are imperative for introducing advancements effectively.

Several interviews in similar studies have highlighted physicians' concerns that precision medicine could harm the physician-patient relationship by causing physicians to rely heavily on data rather than treating the patient as a "whole person" (Erdmann, 2021). Physicians must balance health-focused concerns, ethical considerations, and patient well-being in making their decisions. For example, disclosing disappointing results of precision medicine biomarker tests to patients can cause psychological harm. Physicians demonstrate a desire to address these issues before adopting new practices (Vetsch et al., 2019). Additionally, patients' attitudes toward treatment and precision medicine also significantly influence whether they receive treatment. Many oncologists believe that ordering genetic tests should be a shared decision between providers and patients and do not order genetic tests if their patients are reluctant (Bombard et al., 2014). The quality of individual physician-patient relationships has an impact on a physicians' proclivity to introduce new or experimental practices to these patients. Therefore, improving communication and the quality of individual physician-patient relationships is crucial for introducing new or experimental practices to patients. Overall implementation of new practices would therefore benefit from more comprehensive physician training in communication and increased time spent providing direct patient education.

Precision medicine has gained popularity in the media and among the public, with over 700 appearances in North American media between its implementation in 2005 and 2018 (Marcon et al., 2018). This has positively facilitated its implementation in the clinic. Physician interviews revealed that patients are not only more inclined to follow through with suggested regimens but also frequently bring up genetic testing and precision medicine techniques in conversations with their providers, improving the overall implementation of precision medicine into care. Conversely, the attitudes of some patients have revealed that they are hesitant to receive genetic testing because they fear that having genetic information as a part of their medical record may open themselves up to racial discrimination and harm them down the line in legal issues and concerning health and life insurance, regardless of the current validity of this belief (Erdmann et al., 2021). Race is an influential factor in this feeling, with Black and other minority groups experiencing a much higher likelihood of reporting fear of genetic testing as it

may put them at risk for discrimination (Chakravarthy et al., 2020). Ultimately, a patient-centered approach prioritizing public education, addressing concerns, and promoting equity is crucial for overcoming barriers to the widespread adoption of precision medicine and ensuring its benefits are accessible to all patients.

The environment and relationships in which oncologists work may affect the speed of adopting new practices. Social relationships among doctors have been shown to increase the speed at which new therapies are adopted by physicians and their practices. For example, in a study which comprehensively evaluated 44,000 patient treatment regimens and conducted robust interviews with surveys, researchers found that a chemotherapy drug, Bevacizumab, was more often used by a physician if a colleague they were acquainted with also used it (Keating et al., 2020). Active membership in broader organizations and attendance at research conferences are also associated with greater adoption speed (Bombard et al., 2014). Increasing access to these events and relationships are important, especially for physicians in rural and community practices, to benefit their patients.

Cultural factors and attitudes affecting the adoption of new practices also create inequalities in the speed of adoption among healthcare providers and patients. Physicians' attitudes, as identified in interviews and implementation science studies, point toward several possible focuses for future studies to create more efficient and equitable implementation of clinical practice. While technical and organizational components may be easier to address from a design perspective, it is necessary to consider cultural factors to address inequalities in the implementation of new medical practices, as technological factors cannot easily circumvent this issue.

## Organizational and Technological Level Factors

The second pillar postulated by Pacey's Triangle, organizational factors, is crucial in implementing advancements like precision medicine (Pacey, 1985). Inefficiencies at this level have been attributed as significant barriers to the implementation of precision medicine and are key targets for improvement.

Many patients who receive a positive cancer diagnosis and are eligible for biomarker testing that informs their chemotherapy treatment do not receive this opportunity. A study on a

cohort of NSCLC patients reviewed the process of receiving precision medicine practices and observed which eligible patients were missed due to organizational and physician-related factors. This robust study, using data from over 500,000 patients and validated by international investigative studies, also pinpointed at which step in the process patients were lost (Sadik et al., 2022). The precision medicine treatment process being examined required a biopsy of the patient's tumor, appropriate biomarker testing for the biopsy, and a treatment decision informed by the results of testing. The study revealed that about 23% of patients either were not referred for the initial biopsy or did not have biomarker testing performed on the biopsy (Sadik et al., 2022). Physicians surveyed in a companion study attributed this failure in part to the high cost of the process, testing accessibility, and a lack of awareness of testing (Smeltzer et al., 2020). Patients also were lost along the process due to organizational inefficiencies and barriers to access. As the practice of genetic testing was commercialized, clinical laboratories slowly gained the capability to perform the proper testing. Before it became a widespread and widely recommended practice, the lack of available laboratory testing prevented many practices from implementing precision medicine. Even as biomarker testing has become the best-recommended practice by NCCN and NCI (*Biomarkers Compendium*, 2024), some laboratories still lack the infrastructure for this type of testing, and practices must send samples far distances for sampling, delaying the testing process and subsequent treatment (Smeltzer et al., 2020). This especially affects practices and patients in developing countries and even within rural communities within developed countries. Additionally, failures in the testing process prevented patients from receiving useful test results. In the non-small cell lung cancer cohort, 14% of biopsies performed did not provide sufficient tissue, and biomarker testing could not be performed (Sadik et al., 2022). Often, biomarker testing was not repeated or significantly extended the time to treatment decision, and treatment decisions were made before gaining proper information. The delay of biomarker testing not only prevents timely treatment but often causes physicians to choose treatments without biomarker results, negating the benefits of biomarker testing. While a widespread improvement in access to new treatments would be helpful in bringing the benefits of precision medicine, a more manageable and effective improvement would come in improving education in the referral and biopsy process for physicians and reclassifying such biopsies as emergent cases. Additionally, aiming to reduce costs for labs looking to uptake this new practice and simplifying instructions and practices and instructions for lab technicians may be an option

for companies commercializing the practice. In future implementations of precision medicine, it is even more imperative to clearly define the standards and timeline within this process before adding additional layers of complexity to biopsy analysis to guide future forms of cancer treatment in the future.

The cost of a procedure is another significant factor in the initial adoption of new practices by a physician, and the high cost of biomarker testing has caused hesitation in physicians deciding whether to prescribe it. In adopting new practices there is significant overhead cost in the onboarding of the product and in the individual cost of testing for each patient, which is especially high for new, complex processes like novel biomarker testing. The amount of the initial monetary investment required from the practice often causes a difference in the speed of uptake, especially for small community practices. Providers who are part of large academic institutions, which may use research funding to perform clinical trials, can often onboard and use new techniques more quickly, while those in community practices must wait until the product has been commercialized and they are willing and able to make the financial investment (Hess et al., 2023). This contributes to stark inequity among patients receiving treatment in different regions and practices.

Once treatments become accessible to practices, the high cost of biomarker testing for individual patients remains a significant barrier to the accessibility of the treatment. Interviews reveal that cost is the most important factor in a provider's mind when they decide on testing and treatments for patients. Fifty-five percent of oncologists who were interviewed had refrained from prescribing genetic testing because it is too expensive or because it is difficult to receive coverage from insurance payers (Ciardiello et al., 2016). The high cost of biomarker testing makes the out-of-pocket cost unaffordable for most individuals, so insurance coverage dictates the accessibility of testing and the implementation of precision medicine. Coverage for biomarker testing requires approval by insurance payers, and initial approval is required before any tests are paid for. In order testing to become approved, payers require that the advancement is backed by strong evidence and is medically necessary (Trosman et al., 2017). Insurance payers that were interviewed about covering genetic testing cited a need for genes being tested to be confirmed by substantial clinical trials for them to be covered as non-experimental and proven relevant to patients. Insurance payers require proven clinical utility and medical necessity for

treatments (Dhanda et al., 2020). The requirements for coverage vary widely among insurance payers and create ambiguity for healthcare providers, making implementation more difficult. After insurance payers approve new technology for coverage, there is variability in individual coverage for patients within the same practice. The uncertainty of being able to get patient reimbursement for treatment affects a clinician's decision to prescribe the test to their patients. All physicians interviewed by the Ciardiello group noted that they would be more inclined to encourage test for their patients when the cost decreases and when coverage improves (Ciardiello et al., 2016). The requirements for coverage vary widely among insurance payers and create ambiguity for healthcare providers, making implementation more difficult. While cost is challenging to address, particularly for complex and novel technologies, investing in successful and comprehensive negotiations with insurers from the developer's perspective could significantly improve the uptake of precision medicine for patients who would benefit from it. This could include investing in robust clinical trials to demonstrate the substantial benefits of the procedure, clarifying documentation to meet the standards of insurance companies, and focusing on negotiating approval with insurance payer. Given its importance from the physician's perspective, it is likely that this effort would be worth the research and investment. Another option is to seek legislative support to compel insurance payers to more comprehensively cover biomarker testing costs across a broad range of cases (*Kentucky Health News*, 2023). Additionally, incorporating these efforts into future advancements in precision medicine would ease the burden on physicians and patients, allowing for more rapid benefits to patients

## Conclusion

In summary, the adoption of precision medicine has been influenced by a combination of cultural, organizational, and technological factors. Physicians' relationships with other providers and their patients, as well as their education on advancements, are crucial. Organizational and technological factors such as drug cost, technological infrastructure, and accessibility affect patients' ability to receive timely, state-of-the-art care. These factors collectively shape the landscape of implementation science and precision medicine in the medical field. Upon specific analysis, I recommend areas of focus for researchers and proponents of such technologies to improve the implementation of precision medicine practices efficiently and effectively. I suggest investing in improved physician education on new practices, expediting laboratory infrastructure,

and efforts toward insurance coverage inclusion. These areas of focus will most easily improve the speed of implementation given the complex processes involved in precision medicine and bring the great advancements of cancer research to many patients.

**References**

Ashley, E. A. (2016). Towards precision medicine. *Nature Reviews Genetics*, *17*(9), Article 9. https://doi.org/10.1038/nrg.2016.86

*Bill would require insurers to cover biomarker testing for cancer; expensive screening tool is 'cutting edge,' says sponsor – Kentucky Health News*. (2023, February 10). https://cidev.uky.edu/kentuckyhealthnews/2023/02/10/bill-would-require-insurers-to-cover-biomarker-testing-for-cancer-expensive-screening-tool-is-cutting-edge-says-sponsor/

*Biomarkers Compendium*. (n.d.). NCCN. Retrieved May 6, 2024, from https://www.nccn.org/compendia-templates/compendia/biomarkers-compendium

Bombard, Y., Rozmovits, L., Trudeau, M., Leighl, N. B., Deal, K., & Marshall, D. A. (2014). Access to Personalized Medicine: Factors Influencing the Use and Value of Gene Expression Profiling in Breast Cancer Treatment. *Current Oncology*, *21*(3), 426–433. https://doi.org/10.3747/co.21.1782

Chakravarthy, R., Stallings, S. C., Williams, M., Hollister, M., Davidson, M., Canedo, J., & Wilkins, C. H. (2020). Factors influencing precision medicine knowledge and attitudes. *PLOS ONE*, *15*(11), e0234833. https://doi.org/10.1371/journal.pone.0234833

Ciardiello, F., Adams, R., Tabernero, J., Seufferlein, T., Taieb, J., Moiseyenko, V., Ma, B., Lopez, G., Vansteenkiste, J. F., Esser, R., & Tejpar, S. (2016). Awareness, Understanding, and Adoption of Precision Medicine to Deliver Personalized Treatment for Patients With Cancer: A Multinational Survey Comparison of Physicians and Patients. *The Oncologist*, *21*(3), 292–300. https://doi.org/10.1634/theoncologist.2015-0279

Dhanda, D. S., Veenstra, D. L., Regier, D. A., Basu, A., & Carlson, J. J. (2020). Payer Preferences and Willingness to Pay for Genomic Precision Medicine: A Discrete Choice

Experiment. *Journal of Managed Care & Specialty Pharmacy*, *26*(4), 10.18553/jmcp.2020.26.4.529. https://doi.org/10.18553/jmcp.2020.26.4.529

Erdmann, A., Rehmann-Sutter, C., & Bozzaro, C. (2021). Patients' and professionals' views related to ethical issues in precision medicine: A mixed research synthesis. *BMC Medical Ethics*, *22*(1), 116. https://doi.org/10.1186/s12910-021-00682-8

Gingras, I., Sonnenblick, A., de Azambuja, E., Paesmans, M., Delaloge, S., Aftimos, P., Piccart, M. J., Sotiriou, C., Ignatiadis, M., & Azim, H. A. (2016). The current use and attitudes towards tumor genome sequencing in breast cancer. *Scientific Reports*, *6*(1), 22517. https://doi.org/10.1038/srep22517

Hess, L. M., Michael, D., Krein, P. M., Marquart, T., & Sireci, A. N. (2023). Costs of biomarker testing among patients with metastatic lung or thyroid cancer in the USA: A real-world commercial claims database study. *Journal of Medical Economics*, *26*(1), 43–50. https://doi.org/10.1080/13696998.2022.2154479

Keating, N. L., O'Malley, A. J., Onnela, J.-P., Gray, S. W., & Landon, B. E. (2020). Association of Physician Peer Influence With Subsequent Physician Adoption and Use of Bevacizumab. *JAMA Network Open*, *3*(1), e1918586. https://doi.org/10.1001/jamanetworkopen.2019.18586

Marcon, A. R., Bieber, M., & Caulfield, T. (2018). Representing a "revolution": How the popular press has portrayed personalized medicine. *Genetics in Medicine*, *20*(9), 950–956. https://doi.org/10.1038/gim.2017.217

Pacey, A. (1985). *The Culture of Technology*. MIT Press.

ROGERS, E. M., SINGHAL, A., & QUINLAN, M. M. (2008). Diffusion of Innovations. In *An Integrated Approach to Communication Theory and Research* (2nd ed.). Routledge.

Sadik, H., Pritchard, D., Keeling, D.-M., Policht, F., Riccelli, P., Stone, G., Finkel, K., Schreier, J., & Munksted, S. (2022). Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non–Small-Cell Lung Cancer. *JCO Precision Oncology*, *6*, e2200246. https://doi.org/10.1200/PO.22.00246

Smeltzer, M. P., Wynes, M. W., Lantuejoul, S., Soo, R., Ramalingam, S. S., Varella-Garcia, M., Meadows Taylor, M., Richeimer, K., Wood, K., Howell, K. E., Dalurzo, M. L., Felip, E., Hollenbeck, G., Kerr, K., Kim, E. S., Mathias, C., Pacheco, J., Postmus, P., Powell, C., … Hirsch, F. R. (2020). The International Association for the Study of Lung Cancer Global Survey on Molecular Testing in Lung Cancer. *Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer*, *15*(9), 1434–1448. https://doi.org/10.1016/j.jtho.2020.05.002

Trosman, J. R., Weldon, C. B., Douglas, M. P., Kurian, A. W., Kelley, R. K., Deverka, P. A., & Phillips, K. A. (2017). Payer Coverage for Hereditary Cancer Panels: Barriers, Opportunities, and Implications for the Precision Medicine Initiative. *Journal of the National Comprehensive Cancer Network : JNCCN*, *15*(2), 219–228.

Vetsch, J., Wakefield, C. E., Techakesari, P., Warby, M., Ziegler, D. S., O'Brien, T. A., Drinkwater, C., Neeman, N., & Tucker, K. (2019). Healthcare professionals' attitudes toward cancer precision medicine: A systematic review. *Seminars in Oncology*, *46*(3), 291–303. https://doi.org/10.1053/j.seminoncol.2019.05.001