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Reducing Cost-of-Care in Next-Generation Genetic Sequencing

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Abstract

The cost of care in healthcare settings is rapidly rising, and it is increasingly difficult to decrease these costs without compromising quality and accessibility. This paper aims to investigate methods and potential opportunities for innovation of next-generation genetic sequencing in healthcare decisions and trajectories of care. Using various sources such as medical encyclopedias and peer-reviewed journal articles, this paper explores the ways in which genetic testing became popular in medicine and how genetic testing is currently being used. This knowledge is used to conclude the most likely trajectory of genetics within the field of medicine and its most cost-effective interventions. From this analysis, a possible innovation in the processing of patients' genetic samples arises. By streamlining this process of analyzing the samples and the journey of samples from a patient to specialty lab to provider, we can reduce administrative, travel, and labor costs while expediting the process of receiving results, all of which increase quality and accessibility. This also increases access by making the process more efficient. Through the lens of the triple aim of quality, cost, and access, this paper analyzes a topic in healthcare and offers potential innovations that satisfy the triple aim.

Background Research on Cost-of-Care for Genetic Testing

Oftentimes, there are costs of care well before disease treatment even begins. These costs are associated with the testing and initial appointments to determine the cause of the disease so that an appropriate treatment plan can be established and started. One of these types of costs is genetic testing, which is done for various reasons in the preliminary stages of diagnosis. These genetic tests are costly and can be the source of severe financial burdens to insurance companies and the patient responsible for co-payments, deductibles, and out-of-pocket costs. While

next-generation genetic sequencing is a major technological advancement in medicine, there still exist hurdles in its practical implementation. To understand how one might propose and implement innovations in the field of next-generation genetic sequencing, this paper will cover the history of genetics in medicine, outline the costs associated, and finally delve into possible innovations.

Prevalence and relevance

Providers and researchers have used genetic testing as a tool for decades now, but have seen a dramatic increase in prevalence in the past ten years due to advances and the completion of the human genome project. There are generally two uses for genetic testing when ordered by a physician: identifying the genetic change associated with an existing disease, or identifying a genetic change that suggests a risk for developing a disease in the future. For diagnosis, genetic testing is used to "diagnose a genetic condition if you or your child has symptoms." For prevention, it can be used to determine if "you have a genetic condition that runs in your family before you have symptoms, to learn about the chance a current or future pregnancy will have a genetic condition, [or] to understand and guide your cancer prevention or treatment plan" (Genetic Testing, 2022).

There are three types of genetic tests performed, and they increase in cost as the number of genes tested increases. The first type is a single gene test that, as the name suggests, selects for one gene and sequences it. This provides the physician, or another provider, with information on a single gene. The second type of test is a panel, which selects for and sequences an array of genes that fit into the same category or cluster. This type of test is used in screening for cancer risks and can be used for other traits such as "low muscle tone, short stature, or epilepsy" (Genetic testing 2022). The third type of test is a large-scale test, and this can either be in the

form of exon sequencing– the sequencing of all genetic material that is expressed in DNA– or genome sequencing, which looks at the entire genome of a person. The important takeaway from these three levels of genetic tests is that as more genes are sequenced, the cost of sequencing increases. One study estimates that the cost of sequencing a panel, the second level of sequencing, can "range from $249 to $6,040, with most costing $1,500 to $6,040" (Lynce & Isaacs, 2016) but that testing costs can vary greatly. This cost poses a great financial burden, as it is only the first step in finding the cause of the disease.

Who is affected

Truly, everyone is affected by the high cost of genetic testing because of its potential for widespread use. Genetic testing is used primarily in the diagnosis of disease, but is also used for research that affects the future of human health. Researchers use next-generation sequencing to find drugs that can target specific genetic mutations in hopes of curing genetic conditions like cystic fibrosis and various forms of breast cancer. However, focusing more on the medical diagnosis use of genetic testing, 62% of providers in one survey said that their main barrier to genetic testing was the cost of it (Rahma et al., *Knowledge, attitudes, and perceived barriers toward genetic testing and pharmacogenomics among healthcare workers in the United Arab Emirates: A cross-sectional study* 2020). This impacts both the patient and the provider because while the patient cannot receive the recommended testing for their condition, the provider also cannot diagnose the issue in the way they think is best. This involves more stakeholders in the conversation around genetic testing and who is impacted by its high cost. The gatekeeper to patients having access to genetic testing is the insurance company. Insurers are the ones who choose to cover or not cover medical tests and determine what the price to the patient will be. By following the chain, we can see that the decision-making level continues to trace back to the

source. Doctors try to order the test, patients are made aware of the cost or the insurance company denies the test based on cost, so then we ask why the cost is so high. In the survey of physicians, “91.9% showed a positive attitude regarding availability of genetic testing” but identified barriers to be “the cost of testing (62%), followed by lack of training or education and insurance coverage (57.8% and 57.2%, respectively)” (Rahma et al., 2020). All of this increases the administrative burden, which increases the cost of a test that will never be performed. Overall, this makes the cost-of-care of genetic testing a large issue for multiple stakeholders.

Future (unintended) consequences of the issue

Next-generation sequencing is a tool that has taken decades to develop. If we are not able to properly utilize it, then we as a human collective will suffer preventable deaths and curable diseases. This is a long-term approach to the barrier of cost in next-generation sequencing. As for shorter-term consequences, there are people today who are not receiving the proper medical care because of their inability to afford the expensive genetic test that would drive the proper route of care. One study that discusses this issue in the field of mental health found that “genetic testing may provide information to identify, classify, and discriminate between different stages of the disease or patient subtypes, thereby contributing to the objective of personalized patient care” (Pinzón-Espinosa et al., *Barriers to genetic testing in clinical psychiatry and ways to overcome them: From clinicians’ attitudes to sociocultural differences between patients across the Globe* 2022). If the cost of next-generation sequencing continues to be a barrier to its use, an unknown number of patients (though certainly a high number) will go either undiagnosed, misdiagnosed, untreated, or mistreated.

To briefly discuss the research implications of the cost of sequencing, the cost of research will remain high. This will be a barrier to conducting trials that have the potential to cure disease

and improve patient outcomes. In a journal article titled "The State of Federal Research Funding in Genetics as Reflected by Members of the Genetics Society of America," the two authors discuss the lack of increased funding for scientific-medical research in the United States alongside the increased cost of this research. The article discusses in depth the cost of genetic research and how the high cost discourages organizations conducting this costly research from applying for grants due to the cost of the research being more than a grant would ever cover. For example, the article cites that "it takes a million dollars or more to set up a new junior faculty member at many research institutions" and proposes that cost be weighed against the 'cost' "of not sustaining existing junior, mid-career, and senior faculty who suffer a funding gap" (Rine & Fagen, *The state of federal research funding in genetics as reflected by members of the Genetics Society of America* 2015).

Solution will help the greater good

It makes logical sense that decreasing the cost of care for next-generation sequencing and therefore increasing its prevalence would help the greater good, and there is data to support this logic. Academic medical centers are beginning to increase the use of genetic testing by working with the government to cover these tests. Many hospitals accept Medicaid/Medicare to cover the cost of care for those who meet the federal requirements for each program's enrollment. There are specific rules and coverage benefits from Medicare specifically as this population is of an advanced age, and the expansion of benefits to include genetic testing would greatly improve health outcomes for these already at-risk patients. The issue now lies within administrative processes between physicians, medical centers, and the government (acting as the insurer) to expand the benefits of Medicare. One study looked at academic medical centers and safety net clinics to determine the current methods for paying for genetic tests when ordered by a

physician, and found that most of the cost negotiation was actually happening between the medical facility and the laboratory performing the test. This presents a flip side of the story to the proposed solution of involving policymakers to have the government cover more of the cost of testing.

The journal article discusses how these medical sites "largely worked with laboratories that offer testing for little to no OOP[Out Of Pocket] cost to patients, resulting in relatively few economic barriers to testing" and how they innovated on their own to deliver the best care to patients (Lin et al., *Influence of payer coverage and out-of-pocket costs on ordering of NGS panel tests for hereditary cancer in diverse settings* 2021). The inability of key stakeholders, such as private insurance companies and policymakers acting as insurers for Medicaid, forced innovation on the part of providers to deliver for their patients. The innovation created by providers is only a temporary solution due to the inability of private laboratories to provide "no or low OOP costs if panel testing is not covered (which is the case for most insurers), no-cost cascade testing for family members, and financial assistance programs for low-income patients" (Lin et al., 2021). Therefore, the solution that I propose and will argue for is that providers–meaning physicians, administrative hospital staff, and organizations that provide care–implement their own genetic testing within the organization and can collect the genetic samples, sequence them, and deliver the results all within the same walls of the health delivery site such as an academic medical center.

Society at large would also benefit from decreased cost and increased use of genetic testing because it would enrich the educational experience of students both in high school and higher education. Obviously, increased genetic information would enhance the learning of medical students and those in biology-focused higher education programs, but it would also open

the minds of high school students. Exposing students to diverse options in the science, technology, engineering, and math fields will mold today's learners into tomorrow's leaders in a meaningful way. Additionally, increased knowledge in the form of genetic databases will educate medical students and those in professional clinical studies to be better equipped to face genetic diagnoses in their patients (Kopel, *Clinical genetic testing in medical education* 2019).

Innovation plan addressing Cost-of-Care Issue with Research

This section of the paper delves deeper into proposed solutions to the cost barrier of genetic sequencing, including expanding Medicare coverage of next-generation sequencing, making the technology cost less, and installing the technology in the healthcare facility instead of an off-site laboratory.

Previous and current innovations

The field of genetic sequencing has undergone a rapid expansion in the past two decades, with a significant increase in the last five years with the introduction of CRISPR technology being used in research and medicine. The demand for the use of this technology has forced industry leaders to consider methods of cost reduction to use CRISPR more broadly. The use of genetic testing and CRISPR has become a full industry that functions alongside the healthcare industry in a nuanced space, and the business world is taking notice. An article by Forbes discusses the increase in funding for genetic testing in recent years, saying that “It is estimated that the global genetic testing market value accounted for nearly $13 billion in 2019 and is forecasted to nearly triple by 2026” (Vassev, *Council post: Why genetic screening represents a new frontier for precision medicine* 2021). The article also discusses the innovation of direct-to-consumer genetic tests such as 23andMe, which offers 55+ health results based on an at-home test that the consumer mails back to the company, which sequences the sample in their

laboratory. 23andMe “has raised nearly $800 million in funding and was last valued at $2.5 billion” (Vassev, 2021). The innovation of direct-to-consumer tests has greatly increased the access to genetic testing to more people for a lower cost but is not a complete solution, as these companies do not offer extensive testing of entire genomes.

As the article focuses on innovations, it explains that companies such as Genesight and BiogeniQ have developed whole genome sequencing to fill the need for more complete genetic sequencing for doctors to accurately diagnose and treat genetic diseases. These companies and others are trying to not only offer whole genome sequencing but also create databases that are continuously updated so that the money spent on this testing can stretch as much as possible by being useful in the future.

Proposed solution in detail

The proposed solution is threefold, in order to properly address the issue of the high cost of testing. First, coverage would be expanded for genetic testing, so it can serve as a preventative tool for disease and decrease the cost of disease and illness down the line. Second, install genetic sequencing technology such as Ultima, a startup that has created technology to sequence genes for as little as $100, right in the healthcare facilities so that these organizations may process the genetic samples in the same administrative system that they are collected in. The third and final solution is creating a results-sharing database to stretch the dollars that are being spent on this expensive genetic sequencing, to ensure that no results are wasted, and can be used for future research of treatments and cures.

A committee formed by the US Institute of Medicine said “the insurance concept of what is reimbursable (so-called medically necessary) should be defined to include appropriate genetic testing and related education and counseling, and these genetics services be reimbursed under

health insurance plans" (Andrews LB, Fullarton JE, Holtzman NA, et al., editors, *Assessing Genetic Risks: Implications for Health and Social Policy 7, Financing of Genetic Testing and Screening Service*s 1994). This articulates the first step of the solution of covering the testing with Medicaid to expand the use of testing to more of the population.

Adding in the second and third parts of the solution will put the technology, information, and therefore power in the hands of the providers and patients. "Ultima is the first company to deliver a $100 sequence" (Furchgott, *Can start-ups significantly lower the cost of gene sequencing?* 2022) and with this technology installed in hospitals where the doctors are ordering the tests, faster results will be delivered to providers and patients, thus improving health outcomes. The New York Times article puts it as "what can be applied at the bedside" (Furchgott, 2022) is what matters. The final piece is then using all of this new information to compile a database of genetic information that can be used by providers and researchers alike to better treat patients and also develop treatments and cures.

How it addresses the issue

The solution addresses the issue from multiple angles, which would not only fix current problems, but ideally prevent future problems. Involving policymakers to address Medicaid's lack of coverage for many genetic tests would allow for wider access, one side of the triple aim. Policymakers are also acting as insurers, in this case, to help other stakeholders such as providers and patients to improve patient access to technology that leads to improved outcomes. To incentivize the expanded coverage, healthcare organizations could install the next-generation sequencing equipment on-site and minimize outsourcing costs that come with administrative and logistical costs. An example of this would be the installation of the G4 system, which sequences genetic samples and automatically uploads the results to the Terra platform. Terra was

"developed by the Broad Institute of MIT and Harvard, Microsoft, and Verily—for secondary and tertiary data analysis, storage, and sharing of G4-generated data" (*G4 workflow* 2022). These steps address the issue of first funding these tests by making the tests cheaper for insurers, but also creating a database to stretch the dollars spent, making the cost even more justified (increasing value).

How this plan can be implemented

This plan can be implemented by lobbying for Congress to introduce a bill that will expand coverage of Medicaid for genetic testing. Simultaneously, there can be increased funding utilizing private companies, crowdfunding, or grants to produce and install the technology in healthcare settings. This money would be funneled to Ultima, G4, and other companies that specialize in equipment to sequence genes for a lower cost. Singular Genomics, the parent company of G4, uses private investors for the development and manufacturing of its technology (*Investors* 2022). Ultima Genomics draws funding through companies acting as investors (*About Ultima Genomics*) while Element Biosciences has received funding from only a handful of venture capitalist firms (*Element secures $15 million Series a financing* 2022). Once these technologies are installed in hospitals, and policymakers and insurers have provided the coverage, providers can start ordering tests and contributing to the database of genetic information.

Long-term effects of the plan

The long-term benefits of genetic testing have been clearly demonstrated by a wealth of research done in various clinical disciplines such as mental health and psychiatric care, early detection of and treatment of cancer, screening, and diagnosis of chronic hereditary conditions, and more. The journal article about the use of genetic testing in psychiatric care puts it best:

"New technologies in genetic testing provide important new information about the diagnosis, treatment, and prevention of diseases and are of great value for precision medicine" (Pinzón-Espinosa et al., 2022). A goal of genetic testing is to eventually make precision medicine not only widely available, but also the norm. The New York Times article on genetic testing technology says that "much more research is needed to reach the point where genome sequencing becomes a ubiquitous part of a checkup. But cheaper sequencing is a critical first step" (Furchgott, 2022). This solution will, in the long term, have a positive impact on each aspect of the triple aim, starting with cost. By decreasing the cost of genetic testing, access will increase and the quality of care will also increase, especially for lower-income patients on Medicaid. By improving the care of the most at-risk groups in society, we are improving public health overall and lifting collective health in the long run.

Conclusion

Next-generation genetic sequencing represents an exciting chiasm of science and business as the prospect of personalized medicine becomes more possible. This intersection of all stakeholders in healthcare demonstrates the need for collaboration to realize the potential of advancements in care. Policymakers must expand coverage of genetic testing for Medicaid (and Medicare) patients, and insurers at large can increase their coverage of testing. Providers need to be thoughtful in which tests they are ordering, and patients need to work with their providers to make sure the care they receive is appropriate. Payers, whether it be the insurer, the patient, or another source, need to understand the benefits of genetic testing and work with the technologies offered to increase the number of tests being performed. Technology will continue to be improved so long as the stakeholders believe in its potential. This paper has demonstrated the immense potential for improved quality of care that genetic testing offers and how that can

become a reality in the US healthcare system through increased coverage of testing, new technologies that offer sequencing for a reduced cost, and the creation and maintenance of genetic information databases. With this approach, genetic information can be in the hands of providers and patients, which will improve health outcomes.

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