

COMMENTARY

Building an infrastructure to enable delivery of genomic medicine

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Email: gillian.hooker@gmail.com**Abstract**

To meaningfully address health disparities in access to genomic testing, major developments in the infrastructure to support delivery of care are needed. The current value chain for delivering genomic medicine is fragmented, with poor communication between the stakeholders who order, perform, and reimburse for genetic tests. Standards, connectivity, and scaled expertise are needed to reach more people equitably and achieve healthcare returns on society's investments in genomics. As the costs of genetically-targeted therapeutics and treatments rise, a mature infrastructure to support the delivery of genetic tests becomes critical.

1 | INTRODUCTION

The gap between what we can do to improve health with genomic testing and tailored care and what we actually do continues to widen. Significant disparities in access to testing have been noted across the United States (Williams et al., 2019). Studies of populations drawn from state cancer registries have noted significant disparities across cancer types for which coverage policies are favorable (Kurian et al., 2019). A recent analysis of commercial insurance claims data demonstrated wide variability in utilization rates by state for exome sequencing, noninvasive prenatal testing and multi-gene tumor profiling panels, indicating that disparities in access are not limited to any one specific specialty or disease state (Babu et al., 2020).

Among the most consistently cited reasons for disparities in access to testing are challenges with healthcare provider readiness and clinical workflow (Kurian et al., 2019). These are by no means new challenges, yet we have made little progress in meaningfully tackling them. In addition, it seems unlikely that we will, absent a more foundational infrastructure for nimbly supporting genetic medicine at scale. In 2017, Concert Genetics laid out a vision for a such an infrastructure, connecting stakeholders across the genetic testing landscape—clinicians, hospitals, labs, pharmaceuticals, researchers, governing organizations, health insurance companies, and, most importantly, patients—referred to subsequently as the “Genetic

Health Information Network”. As a first step toward enabling this infrastructure, an annual summit was initiated to convene stakeholders for honest, frank discussions of how to incentivize collaboration toward this end. Drawing on the key learnings of these summits, (Whitepapers—Genetic Health Information Network Summit—Genetic Health Information Network Summit, n.d.) this commentary outlines key infrastructural advancements needed to move from use cases and one-off test specific models of infrastructure toward a mature, comprehensive foundation to support the ever-changing and evolving landscape.

2 | THE VALUE CHAIN

To understand the process of achieving value for genetic medicine, it is helpful to think about the value chain of delivery. “Value chain” is a term used in manufacturing to describe the set of activities required to create a product from start to finish. In the case of genetic medicine, this chain is fragmented across stakeholders. Different stakeholders must each perform separate and distinct tasks in order to provide a valuable service to those who stand to benefit. Today, the hand-off between stakeholders often happens at the expense of the patient, and/or requires a significant level of involvement from the patient.

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Genetic Testing Today: An Inefficient Value Chain

The Fragmented Genetic Testing Value Chain (current)

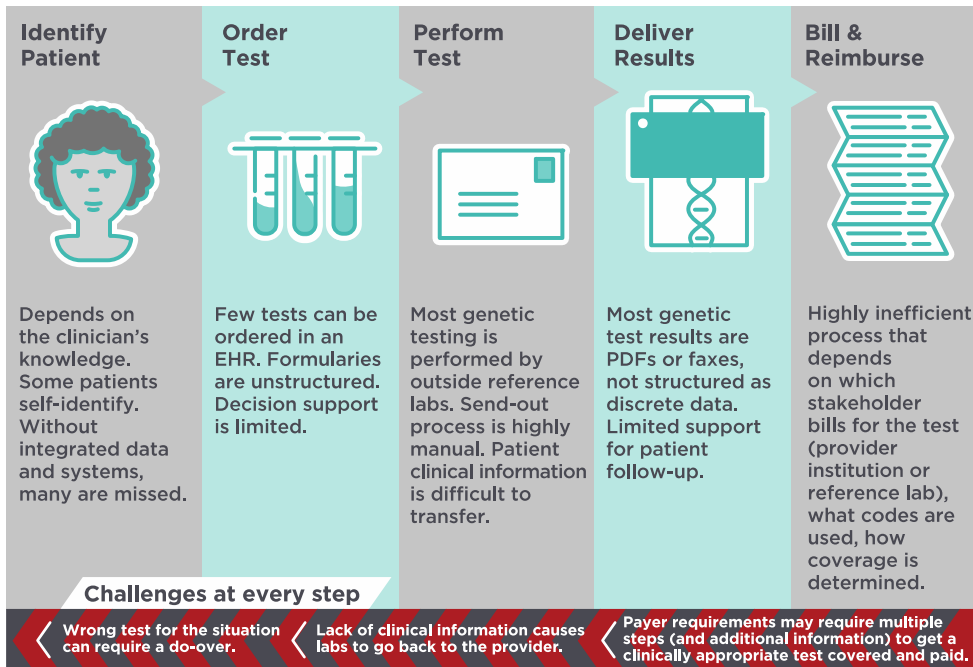


FIGURE 1 Genetic testing today: An inefficient value chain

Figure 1 illustrates this value chain and the ways that stakeholders today interact, across five functional areas. First, patients who will benefit from genetic services must be identified. Today, many of those who see genetic services self-identify. Second, where appropriate, the provider must correctly identify a useful test and place an order. At present, many different paths to order testing are in place and few of them exist within the EHR. Third, samples are usually sent to an outside laboratory to perform the test along with any information necessary to support interpretation of the test, as well as related functions such as billing. Quality of laboratories varies, and few metrics exist to compare between them. Fourth, results are returned to the provider and patient in any number of formats. Rarely, results are stored in the EHR for future reference, and if they are, they may be stored as pdfs that cannot be easily accessed at a later date. Fifth, payment for services is sought, most commonly by laboratories. Reimbursement for similar tests is highly variable, and not transparent to most parties involved in the testing process.

At their core, the problems outlined above with the current system are data transfer problems. Data do not flow efficiently between stakeholders and few standards are in place to support the process. In addition, most, critically, data rarely cycles back to stakeholders in such a way that decisions can be improved upon and learned from over time, creating, as diagrammed in Figure 2, a true value cycle. Solutions have been proposed and tested in each area. When applied collaboratively and comprehensively, the likelihood of delivering value through genetic medicine becomes far greater and we move toward true learning systems.

2.1 | Patient identification

For some time, the field has called upon clinical decision support as a solution to help providers identify patients who need testing. These have been built into the EHR for specific use cases, sometimes requiring patient input, others programmed to fire directly in association with specific drug orders. Unfortunately, few have been conceptualized to keep up with the pace of change of genetic testing and guidelines, rendering most of them obsolete soon after their development. In order to build truly scalable models of decision support standards are needed to define indications for testing, such that data inputs can arrive at an indication for testing, rather than a specific input. This allows for change in the decision support algorithm, independent of a specific test or gene. In such a model standards for describing tests or type of tests can be maintained independently and linked to specific indications in a more dynamic way. To the algorithms themselves, promising high-throughput models of defining patient populations who might benefit from testing or who may have been missed by testing are also emerging (Bastarache et al., 2018).

2.2 | Test ordering

Most provider EHR systems are built on the assumption that someday someone will get around to making sure all necessary send-out tests will be made orderable. In reality, it can take months to years for genetic tests to make it to the top of the priority list, at which time they may not even be on the market anymore. Similarly, many health

FIGURE 2 Vision: An integrated value chain

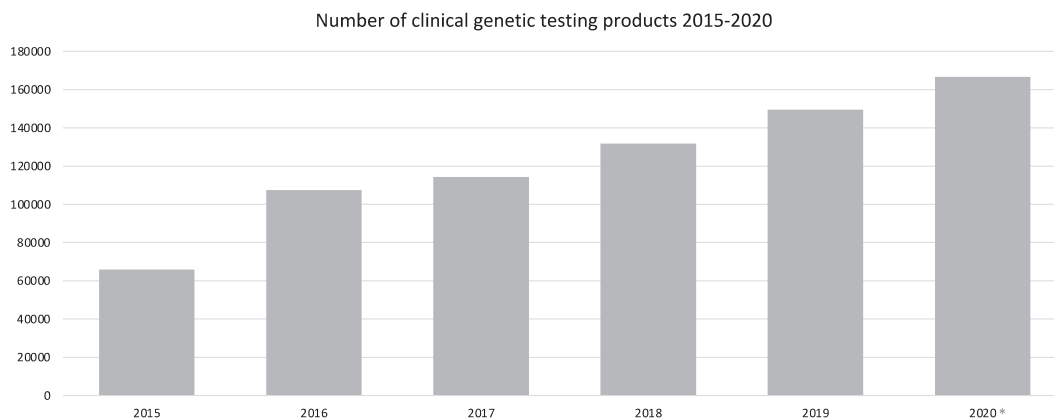
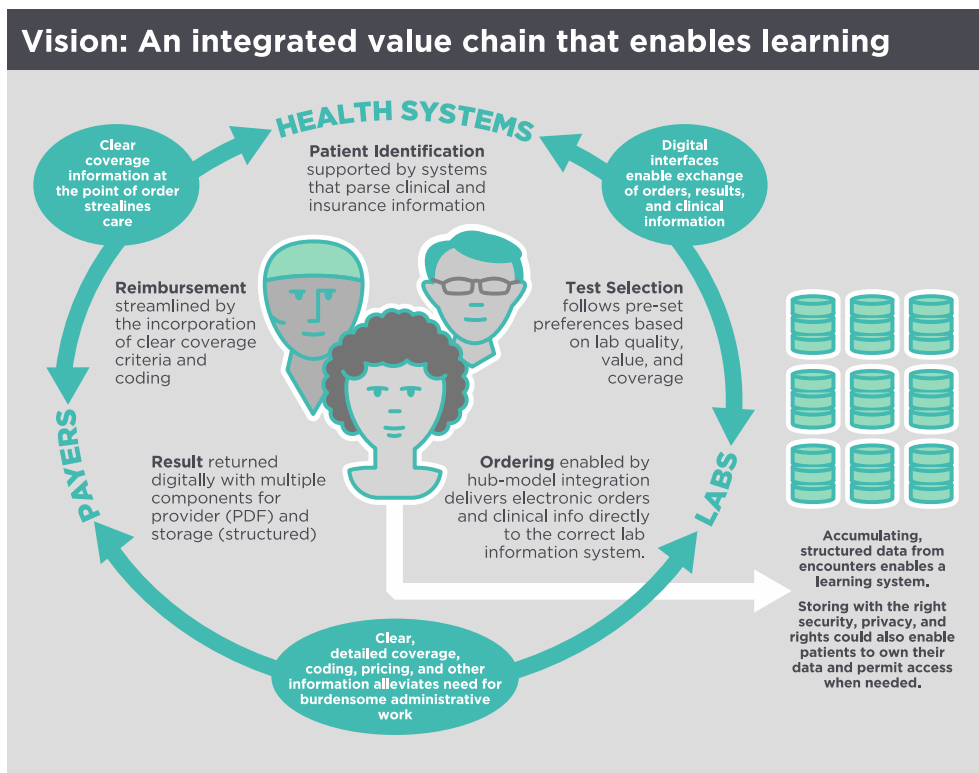


FIGURE 3 Growth in available tests over time. *As of October 1, 2020

systems are setting out to build LIMS-EHR integrations lab by lab to enable smoother flow of information from lab information systems back to the EHR and better data capture between the lab and the provider. The dynamics of the lab industry are such that a health system might end up half integrated with Lab A, integrated with one subsidiary of Lab B, and maintaining a non-functional, out-of-date integration with Lab C.

Further complicating the endeavor of building test ordering into the EHR, lab catalogs are highly dynamic. Since 2015, the U.S. market of tests tracked in the Concert Test Database has grown from 65,893 tests to 166,703 genetic tests currently available for ordering (Figure 3). On average, 22,000 new tests have been added to the market each year. This does not include the tests that have been removed from online test catalogs in this time. Factoring in this rate of growth

and change, it becomes clear that adding tests one by one to an individual hospital formulary is not a sustainable process. It is necessary to build a more sustainable framework around the field of available tests.

In a grocery store, when a new product enters the store, it is placed alongside similar products on shelves that have likely held similar products for longer than the half-life of those products. In much the same way, there is value in adopting a standard taxonomy to describe tests and facilitate comparisons between tests intended for the same purpose. EHR systems can be structured at the category level, allowing individual tests from specific labs to come and go, with stable categories providing an infrastructure and reference point for both clinicians and algorithms aimed at selecting the most appropriate test.

2.3 | Performing tests

In contrast to standard laboratory testing, most genetic tests are sent out to labs that are owned and operated independently of the hospitals and providers caring for the patient. Samples are typically collected by the referring institution and sent to the lab along with a test requisition form and sometimes, additional patient information. In some instances, information is sent both electronically and by mail, and reconciled by the lab upon receipt. Labs rarely have access to the full medical record and must balance between getting the information they need to accurately interpret a test and avoiding a bad customer experience with undue administrative burden on the ordering provider. On the provider side, providers trust that lab will perform the test as intended and interpret the test per existing standards (Richards et al., 2015). CLIA and CAP set minimum standards for laboratory operations, but a mature framework for evaluating test quality, determining when and how confirmatory methods should be used and evaluating the quality of a variant interpretation is still lacking. In addition, there is a limited connection between the cost of a test and metrics of that test's quality. As the market matures, it is critical to better define quality of testing, understand the value of different services offered by the lab, and begin to define sufficiency for particular clinical indications. Overtime, if the market begins to move to a model of onsite wet lab analysis and remote interpretation, defining the value of interpretation services independently of wet lab processes will be of particular importance.

2.4 | Delivering test results

Test results continue to be returned to providers in a multitude of ways. Some results come directly into the EHR, some come back through laboratory portals, and some are still being sent by fax machine. Providers are typically on task to monitor these various inboxes, catch results as they come, scan them, and upload them to the EHR. Today, most hospitals in the U.S. could not determine how many of their patients have had a particular test or gene analyzed. That information is, for most tests, locked in pdfs saved in different places in their patients' medical records, if it is there at all.

Standards for communicating and storing test results are evolving (Zouk et al., 2019) and have been applied for a number of use cases. As is the case with test ordering models, scalable, consistent ways of tracking test results within an EHR from different laboratories have been slow to emerge. Additionally, portability of the results when they are integrated is limited. Absent standards and models for integrating test results, clinical decision support guiding downstream decision-making in a scalable way will also remain confined to specific use cases with specific tests. Here too, there is a need for taxonomy, to group similar test results under common categories, such that as new information is learned about specific variants, variant-drug interactions, variant-guideline interactions, and clinical decision support can be tied to a group of variants, rather than specific variants themselves. The true value of genomic medicine lies in

the downstream decisions that may stem from it, and it is critical that infrastructure support the connection of the results to these downstream activities. Furthermore, we must think about not only a one-time return of results, but ongoing use of those results over time.

2.5 | Test reimbursement

Most tests performed in the outpatient setting are billed under fee-for-service models, usually by the laboratories that perform the tests. The billing landscape for genetic tests at present is characterized by high complexity in the way billing codes are used (ref coding whitepaper), ambiguity in the relationship between the test performed and the codes billed for the test, high denial rates and high administrative burden to both the laboratories billing for the tests and the health insurers paying for the tests. A patient or a provider has little transparency into what a test will actually cost if billed through insurance. Further, given the variability in the way tests are coded, it may not even be clear how policy will apply to a particular test. A plan may list it as a service that is not covered, but be willing to cover it if components of the test are billed vs. billing for the entirety of the test.

This ambiguity has given rise to complex processes of prior authorization, claim review, and appeals that can add 10–20% to the cost of the test for both the laboratory and the health plan just to determine whether it is covered and how much should be reimbursed. Essentially, laboratories and payers are spending a significant amount of money to solve a data flow problem. Drawing on many of the same sort of algorithms one might use for patient identification, the process of determining coverage can and should be a far more automated process than it is today. By applying coverage rules to the type service provided, rather than the CPT codes used to bill for the test, consistency in coverage and payment can be achieved. Providers can determine, at the time of order whether a test will be covered and counsel their patients accordingly and briefly, focusing more of their conversations on the patient's clinical care, and less on complicated insurance processes (Brown et al., 2018).

3 | WORKFORCE CONSIDERATIONS

To adequately meet the infrastructure needs of the population seeking genetics services, a trained workforce is also critical. Studies of physician attitudes toward genetic testing continue to demonstrate persisting discomfort and hesitation in the use of genetic tests (Smith et al., 2020). It may not be necessary for every patient who gets a genetic test to meet with a genetic counselor or medical geneticist, but access to genetics professionals when they are needed is critical, both for patients and for providers seeking a deeper understanding of the tests they are considering. Fortunately, the genetic counseling workforce is growing rapidly. In 2019, the 5,000th genetic counselor was certified by the American Board of Genetic Counseling and the field is on track to double within the next 10 years.

Better reimbursement models are needed here as well. At present, patient-facing genetic counselors are being reimbursed by some commercial insurers for clinical services, but are not yet recognized as providers under Medicare, leading to disparities in who gets access to services and in the quality of care provided to those seeking genetic services. Over time, value should be determined in accordance with patients getting access to the most appropriate pathways for downstream care, including, but not limited to, testing. A test may be a one-time event, but for germline tests, the result persists for a lifetime. Interpretations may change, recommendations may change, and many patients may return to genetic counseling throughout their lifetime. Technology can and should enable genetic counseling services to be delivered at scale, so that all individuals can access services when they most need it, to make decisions that are important for their health and the health of their families.

4 | VISION

With foundational infrastructure in place - standards, connected systems and a sufficient workforce - transformational progress can be achieved. First, such an infrastructure would enable a genetic health information exchange in which patients would not be tied to the system that "owns" their genetic data to get the care they need. Other systems could call down their data when needed, at their request and with their permission. Second, those results could be more easily tied to up-to-date recommendations or actions. Current gene-based guidelines for care and management change on average 2.1 times per year per gene (How Often Do Medical Management Guidelines Change for People with Germline Genetic Findings? 2019). A patient who underwent testing 20 years ago might have lived through dozens of different updates to their management guidelines. That patient and/or that patient's medical record should have an updated feed of recommended actions over time, tied to their test result, made available to them even without having to travel to a center of excellence four states away. Third, and most importantly, an infrastructure for genetic medicine would enable a truly learning system, where necessary data are collected in standard ways, and used to drive iterative improvements in diagnosis and care.

ACKNOWLEDGMENTS

Thank you to Nick Tazik, Rob Metcalf, and Gianna Petrelli for their support in the development of this article.

CONFLICT OF INTEREST

The author of this manuscript is a paid employee of Concert Genetics.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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How to cite this article: Hooker GW. Building an infrastructure to enable delivery of genomic medicine. *Am J Med Genet Part C*. 2021;187C:95–99. <https://doi.org/10.1002/ajmg.c.31881>