



ACCESS:

The First Step Toward Analyzing Precision Medicine Data

When clinicians and translational researchers discuss precision medicine, the conversation often turns to oncology. Cancer is a genetic disease, and a wide variety of genomic determinants influence patient outcomes. For these and other reasons, oncology would appear to be at the cutting edge of precision medicine, since this approach has such clear potential to extend patient lives.

But, as often happens in cancer care, reality is far more complicated than the initial vision. Precision interventions require accurate, timely, and actionable data, and these parameters can pose a variety of challenges.

Whether addressing the entire genome, the exome (the part of the genome with many of the most important DNA sequences), or taking an even more targeted approach, next generation sequencing (NGS), for example, produces a large amount of data. Some of it is useful in a clinical setting; much of it is not. To further complicate the picture, findings that may seem to provide insight into a patient's disease and possible therapies, such as known mutations, may turn out to be “red herrings”—bystander mutations that aren't actually driving the cancer.

Little by little, clinicians and researchers are solving these problems. However, there's an even more fundamental issue

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further upstream: data handling. Before physicians can even begin to judge the value of genomic and other precision medicine data and whether it can help their patients, they need to find, view, and analyze it. Poor access to these data can slow care for cancer patients with no time to waste.

To solve the problem, hospitals and practices must seamlessly integrate precision medicine data into existing systems, such as electronic health records (EHRs). That means replacing manual approaches, which are often slow and prone to error, with digital systems that streamline the process. Sylvester Cancer Center's

ongoing collaboration with software company Syapse illustrates how important it is to have easy access to data. And while administrative refinements may not be as alluring as a shiny new instrument, in this context, they are equally important.

The Importance of Implementing Precision Medicine

At this stage, precision medicine is like a bright teenager who is long on potential but short on productivity. Still, having the ability to precisely characterize each patient's disease, prescribe targeted therapies, and even track the progress of those therapies in (close to) real time is a tantalizing prospect. Medicine must do the heavy lifting to make this happen.

The Sylvester Cancer Center at the University of Miami's Miller School of Medicine is a tertiary referral center that sees patients from the southern United States as well as Central and South America. Many of these patients have relapsed, which means they have already run the gamut of medical, surgical, and radiological interventions. Precision medicine will not help all of them, but it has great potential to help many.

What Holds Us Back

Moving beyond the ability to glean actionable information from NGS and other precision diagnostics, there are critical administrative issues that must be addressed. Sylvester had to find better ways to order precision medicine tests, store the results, and share that information with clinicians and patients. Unfortunately, the old system simply did not produce the results the cancer center—or the patients—needed.

Consider this workflow. After seeing a patient, the physician filled out a paper form to request a test: NGS, FISH, immunohistochemistry, etc. This form was then faxed to the appropriate vendor. Around the same time, pathology would be alerted to provide the appropriate patient samples—yet another link in a quite breakable human chain.

Once the vendor determined the tumor's molecular abnormalities, that report was faxed back to the initiating physician's office. From there, it was scanned and uploaded into the media folder in the patient's EHR. Of course, this folder was already overflowing with documents, making it difficult and time consuming for the physician to even find these important diagnostic results.

In some cases, physicians were required to log in to the vendor's website, or several vendor sites, to view test results. This meant that multiple passwords had to be changed frequently—another administrative burden.

Everything about this process was cumbersome: the paper forms, multiple human interactions, unsearchable documents, duplicative passwords. It was user-unfriendly, but even more importantly, it had the ultimate effect of slowing patient care—hardly the ideal trajectory for precision medicine test results.

Consolidating the Data

To unify this fragmented approach, Sylvester Cancer Center looked at proposals from several software vendors. The solution

had to be easy to use, secure, HIPAA-compliant, and able to provide ready access to patient data. Following a rigorous process, we chose to embed Syapse into our EHR. We were impressed by the comprehensiveness of its offerings.

The Syapse software is the behind-the-scenes engine that transmits information between physicians, pathology, and vendors and ultimately places precision medicine data into the patients' EHR. Syapse has created a digital conduit that securely moves information between the various players. This has had a remarkable impact on the administrative workflow of ordering and reviewing precision medicine diagnostics at our cancer program.

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Compare this to the previous scenario. The physician sees a patient in the clinic and decides to order tests. Instead of filling out a paper form, the provider can now order the appropriate tests using dropdown menus inside the patient's EHR. The system handles the rest, communicating with the vendor and requesting tumor samples from the pathology lab.

A few days later, the patient is back in clinic, and the test results, quite possibly from more than one vendor, are available in the EHR. The data is searchable and annotated by vendor and test type. The physician can easily bring up the information using a familiar interface and just one password. Armed with these results, the provider can discuss therapeutic options with the patient.

The Fruits of Improved Process

Many of the advantages of moving to an electronic system are obvious. The new approach accelerates results, simplifies processes, makes life easier for physicians, and has tremendous potential to improve care.

In addition, setting up this platform opens a wide range of research and clinical options that were unavailable under the old, manual system. Since the information is digital, it gives clinicians a more powerful tool to analyze patient data. For example, this new approach is helping drive a clinical trial called Defining Platforms for Individualized Cancer Treatment (DePICT), which seeks to better define how personalized medicine can improve care. With access to more granular population data, the cancer center can analyze patients who were treated with various precision medicine approaches, look at the outcomes, and determine the utility of each intervention.

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Figure 1. Paper and Pen Workflow

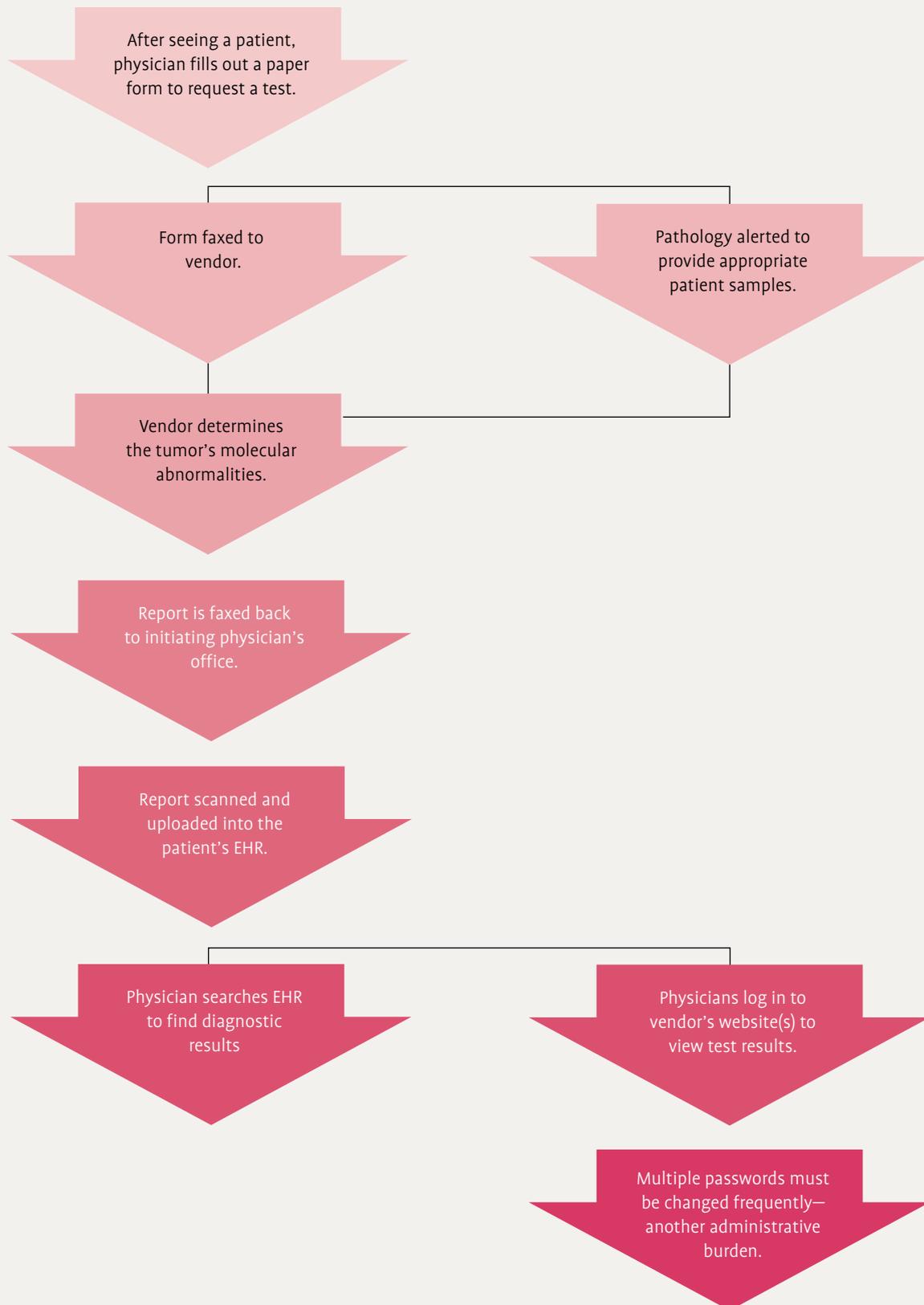
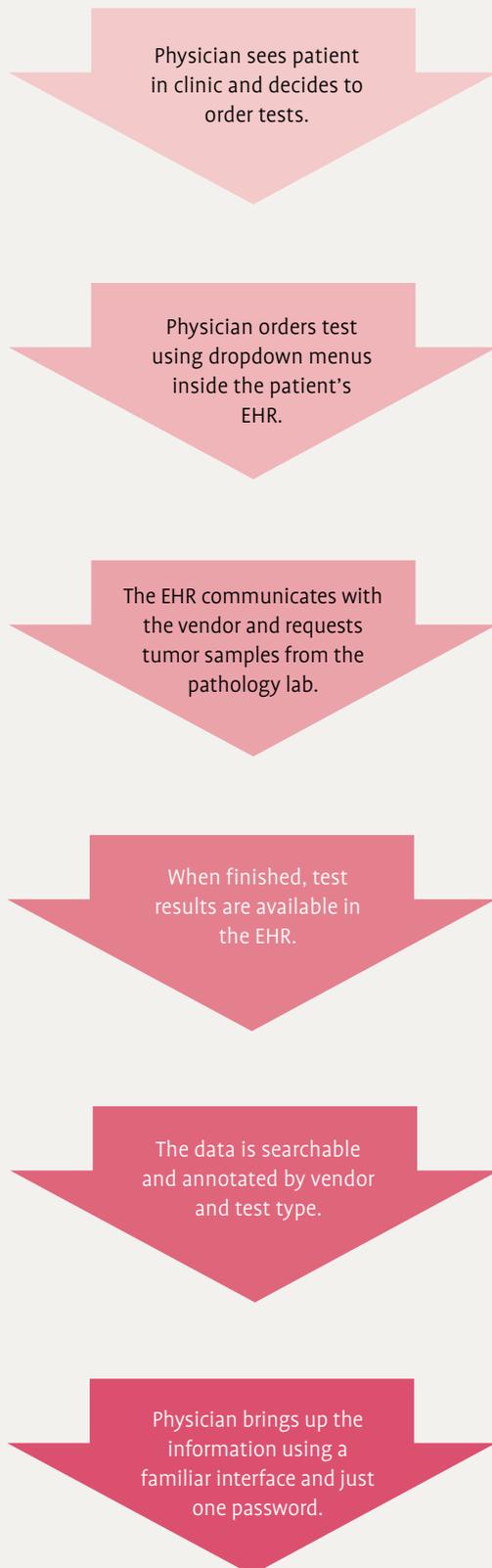


Figure 2. Digital Workflow



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Though it's early days, so far, the data is indicating that precision medicine diagnostics and targeted therapies are improving patient care. Approximately 30 percent of Sylvester Cancer Center's patients are having their treatments modified by precision medicine. In addition, at least one or two patients each month are gaining access to clinical trials. Rapid access to these critical diagnostics helps determine whether a patient qualifies for a trial. Quite often, these patients have no other therapeutic options.

In addition, having access to population data has been enormously helpful when designing clinical studies. Researchers can now slice and dice patient data to better understand which mutations are driving Sylvester patients' cancers. If the data shows a pattern of PI 3-kinase mutations, it provides an additional layer of evidence to support new trials to study PI 3-kinase inhibitors.

Being able to dive into this data, find patterns, and isolate specific patient groups can produce life-saving outcomes. Because of Sylvester's location and expertise, our clinicians see many patients from Central and South America, quite a few of whom suffer from gastrointestinal stromal tumors. In most cases, these cancers are being driven by KIT mutations. However, the population data has shown that a small percentage of gastrointestinal tumor patients have RAF mutations. This information led us to using RAF inhibitors in one patient.

Once again, detailed information provided additional power to help a patient. Because this subgroup was so small, it's unlikely we could have designed a sufficiently powered clinical trial. Importantly, for this patient, the RAF inhibitors helped. We might never have gone down this path if we did not have easy access to the data.

Putting Everything Together

Precision medicine diagnostics are important, but they cannot live by themselves. Physicians still need to bring in treatment history, pathology, radiology, and other data to get the most complete picture of each patient's unique cancer.

To do that, Sylvester has created a precision medicine tumor board, which leverages the expertise of surgical, medical, and radiation oncologists, traditional and molecular pathologists, and others to determine the most appropriate interventions.

The tumor board adds significant context to the precision medicine results. For example, the tests may indicate a patient could benefit from an EGFR inhibitor. However, the patient's treatment history may show that clinicians have already tried this approach—perhaps more than once—and it failed. Precision medicine must always be tempered with real-world observation.

The tumor board's ability to gather and analyze evidence from different sources helps in many ways. Sometimes, when a patient has run out of clinical options, the case must be made to get him or her into a clinical trial under compassionate use guidelines. This can be a steep hill to climb, but information from the tumor board is often quite helpful in making that case.



Courtyard of the Sylvester Comprehensive Cancer Center at the University of Miami, Miami, Fla.

A Teaching Moment

Molecular medicine is such a new area that most patients have no idea what it means. Patients need to learn how these data influence their treatment options and ultimately their lives. In some cases, patients have no experience with the most central concepts: What are mutations? How do they drive cancer? How can a specific class of inhibitor turn the tide?

Most physicians do not have the time to explain these details to every patient, so Sylvester created a precision medicine clinic. Faculty and nurse practitioners help patients understand their cancer, how mutations in a tumor genome drive their disease, and how precision medicine tools can both identify and fight specific mutations. In addition, patients learn about immunotherapy, targeted treatments, and many other aspects of cancer care.

Once patients understand the basic framework, it becomes much easier for the nurse practitioner to go over their test results and explain how those impact their treatment options. The clinic makes patients more comfortable with the bold new world of precision medicine. Acronyms like EGFR, RAF, and KIT become meaningful, and that helps patients ask more probing questions and incorporate the answers into the decision-making process.

Looking Ahead

Molecular medicine is moving rapidly. Today's *Nature* paper could ultimately be tomorrow's diagnostic. It's important to find ways to integrate these new findings into patient care, but it's even more important to do the necessary research to ensure these tests improve outcomes.

That's why the data is so important. As each shiny new diagnostic gets added, clinicians and researchers must ensure its accuracy and carefully delineate which patients benefit. Having

access to population data from a single cancer center, a region, a nation, or the entire world will vastly improve the ability to make those determinations.

Sylvester's new partnership with Syapse has shown us that precision medicine is being used more frequently and that these approaches are, overall, improving care. Sylvester is now in a much better position to explore other modalities, such as using circulating tumor DNA to detect recurrence and adjust therapy accordingly. This approach is not quite ready for prime-time, but having greater access to molecular data could accelerate its adoption.

Data will also support efforts to further define which patients will benefit from emerging immunotherapies. Equally important, it could outline which mutations defeat these exciting therapies and point to new ways to turn cold tumors that do not respond to treatment into hot ones.

Precision medicine has a long way to go to meet its potential, but one way to speed this process is to implement the right information technology systems to maximize its benefits. Archaic paper forms, unsearchable data troves, and other barriers can slow progress and ultimately hurt patient care. Creating a digital conduit between caregivers and vendors expedites results and liberates the data for research and other applications. Putting this system in place has been an important milestone in Sylvester Cancer Center's efforts to maximize precision medicine's utility. 

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