



Building a continuous-learning system: the utility and value of integrating genomics and outcomes registries into clinical practice

Oncology care exists in a dynamic environment of rapidly evolving health technology, increasing complexity and cost of care, and continuing skepticism about whether rapidly introduced tools such as genomic profiling result in clinically significant improved outcomes. The introduction of new technologies and therapies (e.g., genomic testing, targeted therapies, and immunotherapy) on a faster regulatory track based on studies of smaller, stratified patient populations has led to a demand for a broader evidence base to inform clinical practice, particularly with respect to precision medicine in oncology.

Many stakeholders are now leveraging the joint capabilities of genomics and health information technology (HIT) to build that evidence base. Under the aegis of a genomics-driven, continuous-learning model,¹ some industry leaders are working with clinicians, health system executives, payers, and others to collect real-time clinical data. This data will drive scientific discovery, shape clinical practice, and enable more informed discussions on efficacy and cost effectiveness in care delivery. On November 3–4, 2015, led by the Sustainable Predictive Oncology Therapeutic and Diagnostics (SPOTDx) working group,² leaders from a number of healthcare institutions gathered to discuss several of these collaborative efforts. Those efforts include:

- NCI-MATCH (Molecular Analysis for Therapy Choice)
- SPECTA (Screening Patients for Efficient Clinical Trial Access, a program of the European Organisation for Research and Treatment of Cancer)
- The Molecular Evidence Development Consortium (MED-C)
- The Targeted Agent and Profiling Utilization Registry Study (TAPUR)
- The Syapse-Intermountain collaboration
- Geisinger's MyCode Community Health Initiative

¹ Under a continuous-learning model, data routinely generated through clinical research and patient care feed into what Dr. Amy Abernethy describes as “an ever-growing data bank or set of coordinated databases.” Describing how the system learns, she says, “The system ‘learns’ by routinely and iteratively: (1) collecting data in a planned and strategic manner; (2) analyzing captured data; (3) generating evidence through retrospective analysis of existing data as well as data from prospective studies; (4) implementing new insights into subsequent clinical care; (5) evaluating outcomes of changes in clinical practice; and; (6) generating new hypotheses for investigation.” (Amy Abernethy, “[Rapid Learning Cancer Care: Getting Serious About Implementation.](#)” *Health Affairs Blog*, July 29, 2010). Thus information, purposefully obtained in real time in the course of routine clinical practice, drives the process of discovery and ensures that a focus on continuous innovation, quality improvement, safety, and value is intrinsic to the healthcare system.

² In 2013, a premier group of healthcare leaders from across the United States launched the Sustainable Predictive Oncology Therapeutics and Diagnostics (SPOT/Dx) Working Group. SPOT/Dx is a multiyear effort focused on improving patient outcomes by equipping healthcare leaders with tools to advance clinical decision making, the diagnosis and treatment of cancer, and the regulatory and reimbursement infrastructure that underlies the field of precision medicine. For more information please see “[Sustainable Predictive Oncology Therapeutics and Diagnostics \(SPOT/Dx\) Working Group.](#)” Tapestry Networks, 2015.



Meeting participants identified similarities, differences, gaps, and potential synergies across these initiatives. They questioned, *“How do we optimize the learning we get from these studies? What evidentiary requirements are needed to support the useful and meaningful practice of genomic medicine?”*³ Participants also explored ways to bridge research and clinical care in service to oncology patients seeking improved health outcomes. This synthesis integrates the November meeting discussions as well as post-meeting debriefs across participants and the broader landscape of stakeholders. See Appendix A for list of participants and contributors to the discussions. It highlights key themes (listed below) and details potential next steps:

- **Next-generation sequencing (NGS).** The excitement and interest in NGS is palpable, but questions remain about its *“readiness, usefulness, and impact”* on clinical care management and patient outcomes. Understanding the evidence that is being generated across a landscape of genomic-driven studies is a critical step in addressing these questions. (Page 2)
- **The quality and reliability of technological and clinical data.** Healthcare leaders must improve the quality and reliability of technological and clinical data before value can accrue from genomics-driven studies. (Page 6)
- **Data sharing.** The ability to share data across initiatives may be useful where there is an overlap in data elements, shared nomenclature, and agreed standards. (Page 7)
- **The importance of leadership and incentives.** The challenges of integrating genomic tools into a continuous-learning system are not problems of technology but of leadership, incentives, and will. (Page 8)
- **Progress on oncology outcomes.** Progress on oncology outcomes will require integrated solutions that include, but do not solely depend on, genomic tools. (Page 9)
- **The necessity of new models of leadership and collaboration.** New models of leadership and collaboration are needed to advance the genomics and real-world registry agenda. (Page 10)

Next-generation sequencing (NGS)

Several leaders in oncology suggest that molecular targeting and diagnostic profiles (e.g., next-generation sequencing) will enable individualized therapy with improved benefit-risk ratios. They laud the potential for biomarker profiles to define treatment benefits not only for individuals, but also for certain patient cohorts. The number of targeted oncology drugs available is increasing, as is the number of patients getting NGS panels. Additionally, the costs for capturing and coordinating data are lower than in the past thanks to the HIT infrastructure available to many facilities today.

However, it is unclear whether NGS technology is ready for use in the everyday practice of medicine. One researcher commented, *“I’m not sure NGS is ready for prime time in the clinic. It needs to be done in the*

³ *ViewPoints* reflects the use of a modified version of the Chatham House Rule whereby comments are not attributed to individuals, corporations, or institutions. SPOT/Dx Oncology Summit participants’ comments appear in italics.



context of a research study. We should discourage doctors from profiling patients and prescribing drugs in the context of routine clinical care, where it remains an unproven strategy. Instead, we should encourage patients to participate in the available clinical trials that can help inform the whole discussion.”

Currently there are several studies under way that use genomic tools to understand disease progression and identify treatment options for oncology patients. These studies promise to generate the evidence needed to make clinical use of molecular profiling possible and practical. If successful, these studies will highlight the utility of NGS as a tool for classifying disease appropriately. An industry leader described the value of these data-gathering efforts in staging cancer: *“I don’t think the primary use of genomics is to immediately find a targeted drug. It’s actually to understand the disease at the molecular level, at a level of detail that we never had before. We are really at a new world where we are literally redefining disease and going beyond pathology, beyond the classic physical view of stage. We are defining it at the molecular level. Some of these trials I hope will capture that information.”*

Questioning NGS’s clinical utility in a real-world setting

Several healthcare leaders questioned the implicit assumption of value for NGS without a body of supporting evidence. A payer asked, *“Is the NGS approach actually useful in identifying specific populations of patients with specific indications of specific clinical scenarios who would benefit, right, from taking that approach? If so, what is that population? How do we identify that population? And then to take that one step further, is [NGS] actually better than what we’re doing now? Better than the current standard of care?”*

Recent reports from the SHIVA study support this skepticism. SHIVA was a randomized, controlled phase 2 trial designed to assess the efficacy of several molecularly targeted agents marketed in France. The agents were chosen on the basis of tumor molecular profiling but used outside their indications, in patients with advanced cancer for whom standard-of-care therapy had failed. Results of the study, published earlier this year in *Lancet Oncology*, showed no significant difference in progression-free survival between patients randomly assigned to receive molecularly targeted agents used off label on the basis of the molecular profile of the tumor and those assigned to receive therapy based on the physician’s choice.⁴ Patients receiving targeted therapy had a median progression-free survival of 2.3 months, compared with 2.0 months for patients receiving therapy based on the physician’s choice.⁵

Whether or not participants believe NGS is ready for prime time, most agreed that a prime reason to conduct these studies *“is really to tell us as quickly and efficiently as possible what doesn’t work as much as ... what does work so you can at least sort of get rid of the approaches and therapies and indications and so forth [that] clearly [are] not going to help.”*

Some asked whether the healthcare system should be a tool for discovery (as opposed to a place to apply evidence-based approaches), but whatever their misgivings, participants agreed that the time to question the introduction of NGS into health systems has passed. A health system leaders summarized: *“NGS testing is*

⁴ Christophe Le Tourneau et al., [“Molecularly Targeted Therapy Based on Tumour Molecular Profiling Versus Conventional Therapy for Advanced Cancer \(SHIVA\): A Multicenter, Open-label, Proof of Concept, Randomised, Controlled Phase 2 Trial,”](#) *Lancet Oncology* 16, no. 13 (October 2015), 1324-1334.

⁵ [Ibid.](#)



the train that's left the station. It's running; it's going fast. There's going to be a ton of data; there's going to be a ton of issues. We have to find a way to capture that data. It won't be perfect, but it will be useful." Time would be well spent leveraging these studies to provide clinical utility and outcomes data. A payer noted, *"You can't put the toothpaste back in the tube. We can either pay for this stuff passively or support efforts to generate data that will prove or disprove its utility here."* Another payer pleaded, *"Help clarify the black box that is genomic data analysis."*

Understanding the landscape of genomics-driven studies in service to evidence-based medicine

Given the shift to outcome-focused payment systems in healthcare and increasing considerations of value, benefit-risk, and affordability, genomic tests need to prove their worth in terms of real-world outcomes for patients, which means that innovative approaches to evidence generation and data analysis are needed to match the changing landscape in oncology. Among the portfolio of evaluative approaches are retrospective analyses, prospective studies, clinical trials, and comparative-effectiveness studies.

According to a National Cancer Policy Forum report, a continuous-learning system can deliver "understanding of clinical effectiveness for ... individuals with multiple comorbidities and those on concomitant medications frequently excluded from clinical trials; comparison of multiple anticancer drug combinations ... ; the predictive value of unexpected associations ... ; [and] retrieved information on the historical experiences of similar patients that could help guide treatment choices for a current patient."⁶ Several institutions have recently designed and/or launched genomic-medicine initiatives utilizing the continuous-learning model, including the following:

- **SPECTA (Screening Patients for Efficient Clinical Trial Access)** is a pan-European network built by the European Organisation for Research and Treatment of Cancer (EORTC). Key institutions collaborate to provide patients with efficient access to molecularly driven clinical trials. Through SPECTA, oncologists can now allocate patients to clinical trials based on both their clinical characteristics and the molecular profiles of their tumors. Going a step further, they can help identify new subgroups of tumors. This EORTC research program also provides the opportunity to conduct further research that might lead to the identification of new biomarkers or help in the planning of future clinical trials. In its explanatory brochure on SPECTA, EORTC says, "Disease-specific screening platforms for colorectal, lung, melanoma, brain, and rare cancers optimize drug access, precision medicine, and new healthcare delivery. To date, the SPECTA platforms for colorectal cancer and thoracic tumors are fully operational."⁷
- **Molecular Evidence Development Consortium (MED-C)** seeks to complement traditional randomized, controlled trials with the real-world evidence needed to demonstrate clinical utility. MED-C proposes to increase precision medicine's evidence base and streamline the diagnostic process (thereby reducing cost) by investigating promising molecular interventions as early in the treatment pathway as possible for patients who are outside the clear standard of care. It will use targeted medicines donated by

⁶ Amy P. Abernethy et al., "[Rapid-Learning System for Cancer Care](#)," *Journal of Clinical Oncology* 28, no. 7 (September 2010), 4269.

⁷ European Organisation for Research and Treatment of Cancer, [SPECTA: Screening Patients for Efficient Clinical Trial Access](#) (Brussels: European Organisation for Research and Treatment of Cancer, 2015), 1.

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pharma and create an outcomes registry. Like randomized, controlled trials, MED-C aspires to generate robust prospective data through strict adherence to treatment protocols. It has received funding to launch its first registry in non-small-cell lung cancer.⁸

- **Targeted Agent and Profiling Utilization Registry Study (TAPUR)** seeks to address the lack of evidence surrounding off-label oncology treatments. TAPUR is a prospective, non-randomized clinical trial that aims to determine the safety and efficacy of commercially available, targeted anticancer drugs for treatment of patients with advanced cancer that has a potentially actionable genomic variant. Supported by the American Society of Clinical Oncology (ASCO), the study intends to simplify patient access to approved targeted therapies that collaborating pharmaceutical companies contribute to the program. The study will catalog which genomic profiling tests clinical oncologists choose and provide evidence on the utility of registry data in developing hypotheses for additional clinical trials. ASCO will launch the TAPUR study at clinical sites involved in the Michigan Cancer Research Consortium, the Cancer Research Consortium of West Michigan, and the Carolinas Healthcare System – existing research networks that run research trials for the National Cancer Institute (NCI) and industry – with the ultimate goal of expanding nationally.⁹
- **The Syapse-Intermountain collaboration** integrates complex genomic and clinical data to provide clinicians with actionable insights at point of care, enabling diagnosis, treatment, and outcomes tracking. A genomics cancer medicine pilot program will provide patients with precision cancer medicine and determine whether a genomics-based cancer treatment approach yields superior outcomes. Testing will serve patients with stage 4 cancer for whom traditional treatment methods have been unsuccessful.¹⁰
- **NCI-MATCH (Molecular Analysis for Therapy Choice)** is a novel “bucket” clinical trial design that aims to streamline clinical development through rapid screening of patients and channeling to multiple trials. The phase 2 trial seeks to determine whether targeted therapies for people whose tumors have specific gene mutations will be effective regardless of their cancer type. It will incorporate more than 20 different study drugs or drug combinations, each targeting a specific gene mutation, in order to match each patient in the trial with a therapy that targets a molecular abnormality in their tumor. The trial is codeveloped by the NCI/National Institutes of Health, ECOG-ACRIN Cancer Research Group, and the NCI-sponsored National Clinical Trials Network. The trial opened for enrollment in August 2015 with 10 arms. Each arm will enroll adults 18 years of age and older with advanced solid tumors and lymphomas that are no longer responding (or never responded) to standard therapy and have begun to grow. Additional arms are expected to open for enrollment early in 2016. NCI-MATCH investigators plan to obtain tumor biopsy specimens from as many as 3,000 patients initially.¹¹

⁸ For more information, see [“Molecular Evidence Development Consortium: Harnessing the Strength of Many to Unlock Cures One by One.”](#) the MED-C website.

⁹ For more information, see [“About the TAPUR Study.”](#) the TAPUR website.

¹⁰ For more information see Andro Hsu, [“New Studies by Intermountain Healthcare’s Intermountain Precision Genomics Reveal that Precision Medicine Improves Survival in Advanced Cancer Patients without Increasing Costs.”](#) Syapse blog, May 29, 2014, and Andro Hsu, [“Intermountain Healthcare and Syapse Collaborate to Improve Access to Clinical Genomics for Community Oncologists.”](#) Syapse blog, May 29, 2014.

¹¹ For more information, see [“NCI-Molecular Analysis for Therapy Choice \(NCI-MATCH\) Trial.”](#) National Cancer Institute, October 30, 2015.



- **MyCode Community Health Initiative**, a precision-medicine program from Geisinger, has created a biobank to which more than 50,000 Geisinger patients have consented to donate blood and/or tissue samples for sequencing. Participants also give researchers permission to access their medical records to aid in the investigation of new approaches to disease control, prevention, diagnosis, and treatment.¹² The study uses a broad consent and includes the ability to recontact participants. Geisinger installed electronic medical records 19 years ago, and a median of 12 years of data are available for biobank participant. The program has committed to returning medically actionable research results, including on inherited cancer syndromes (breast, ovarian, and colorectal). As part of a partnership with Regeneron Pharmaceuticals, MyCode currently plans to collect and sequence samples from more than 250,000 consenting patients.¹³

When producing evidence through a continuous-learning system, “it is important to match study design with the importance and complexity of the research question, balancing rigor against the need to generate timely generalizable evidence.”¹⁴ While the randomized, controlled trial is still the definitive methodology for answering efficacy questions and must therefore continue to hold a central position in the clinical/research system, the studies listed above suggest a role for the use of genomic information in innovative clinical trials.

Recognizing that successful early experiences can inform subsequent efforts, the SPOT/Dx working group brought together several innovators from these efforts to describe their ongoing projects and challenges, identify common infrastructure and research needs, discover where there are gaps, and consider what solutions are required to optimize the value of data generated across the field.

The quality and reliability of technological and clinical data

Participants agreed that genomics-driven studies inhabit a highly variable environment in terms of quality and reliability on two critical dimensions: (1) technical aspects of diagnostic platforms and associated pre- and postanalytics, and (2) clinical data. A lab director commented on the vast differences in the quality of data being produced by various NGS labs: *“The variability for some labs is not only at a technical level or assay design level. Some of these assays are little more than multiplex PCR [polymerase chain reaction] assays, all the way to comprehensive tests, the hybrid capture that go all the way to whole exomes and whole genomes. Given that we’re all here to improve patient care, if the data that you’re working from is uneven across laboratories, it’s going to be very difficult to come up with any meaningful outcomes-based data.”*

A clinician stressed the clinical aspect of the quality problem: *“A lot of the discussion today is focused on the quality of the genomic data, but I will assure you that the quality of the clinical data is every bit as important, maybe more important, and every bit as difficult to get reliability on as the genomic data because to some extent the clinical data is in many cases filtered through the eyes of the clinician, and it’s not necessarily as objective as some of the genomic data might be.”* An industry leader advised the group to investigate the rigor with which diagnostic tools are selected as well as the quality of data collection from electronic records

¹² For more information, see [“MyCode Community Health Initiative.”](#) (partnering-with-patients page) Geisinger, 2015, and the MyCode paragraph at [“Genomic Medicine Institute.”](#) Geisinger, 2015.

¹³ [“MyCode Community Health Initiative.”](#) (initiatives-and-projects page), Geisinger, 2015.

¹⁴ Abernethy, [“Rapid-Learning System for Cancer Care.”](#)

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and other databases. *“There’s often a tension between clinical research and clinical management. Our objectives in each area are different, and therefore the respective quality considerations are different.”*

Participants recognized the struggle to balance the quality of technical tools and data against the quality of clinical information obtained. *“How do you strike the proper balance of the real-world setting against the ability to get good data?”* one asked. A regulator suggested that accepting less-than-sterling data in exchange for practical usability could be a worthwhile trade-off: *“We as a community need to acknowledge that there are certain kinds of data sets that we may wish to use for clinical decision making that simply will not be as reliable as what we’re accustomed to seeing from clinical-trial data sets. And that is a fact of life. It doesn’t mean that they’re not useful or informative.”*

Clinical-trial designers pointed out that the highly reliable data sets from clinical trials have drawbacks too: *“The patients in those trials are so poorly representative of the patients that we actually treat in the real world.”* In fact, one member suggested that clinical-trial data and real-world data are in fact *“complementary data sets. You have got the data from the clinical trials that give you a certain level of quality, a certain level of reliability and confidence, but may not be applicable to most people who are going to be exposed to that product, whether it is a drug or a device or whatever, once it is out in the marketplace. And then you’ve got the more real-world data, which is dirtier, maybe less reliable, less reproducible, but perhaps more representative of what is going on in the population of interest. You need both sets of information to make an informed judgment.”*

Data sharing

Participants agreed on the value of sharing data in principle: data sharing makes it possible to optimize learning by mining larger pools of aggregated data. An industry leader commented, *“We’re at the beginning stages of the genomic Internet, in which you can create a massive amount of genetic information across every patient and [in] the way in which we actually store that data and share that data. As a company, we are huge on the value of data sharing, which I think is also a new business model that’s emerging in biotech.”*

A regulator described similar interest from the Food and Drug Administration (FDA) on the data-sharing agenda, saying that the efficiency derived from data sharing, combined with the opportunity to draw more meaningful conclusions from a pooled data source, *“is certainly useful. At the FDA, we’ve been putting a lot of thought into how we can shift from a reductionist approach to precision medicine (one drug, one gene) to a more holistic approach when looking at these integrated data systems where data is standardized and shareable.”* Regulators recognize the benefits of an interconnected system: *“Interconnected data systems will allow us to answer questions a lot more efficiently. The goal is not to have perfectly clean data and perfect systems. There are methods, scientific methods that can be applied to reduce uncertainty. And that’s really what we need to strive for.”*

However, one payer raised some questions: *“What data should be collected? What data should be shared? How would we facilitate this through standards of interoperability?”* Given the range of data collected, the variety of molecular tests used, and the scope of data elements in use, one clinician suggested leaders of the



case studies presented convene in a separate setting to share and discuss the data elements each is incorporating as well as the nomenclature each is assigning to its study. This would provide a starting point from which common data-sharing mechanisms could be derived. As one industry noted, *“Data sharing is powerful. Before jumping into the data, we should ask, is the data worth sharing in terms of quality and scope?”* An HIT leader added, *“Can we cultivate ‘FAIR’ data [findable, accessible, interoperable, and reusable]? How do you get genomic data to flow in the EMRs [electronic medical records]? How do we structure the data in a way that is sharable?”* A number of participants supported the proposal to identify shared data elements across the studies, with one HIT leader stressing that the *“synergy from a common methodology and nomenclature will allow these efforts to talk to each other more effectively.”*

Defining a shared nomenclature

Participants discussed the futility of data sharing without a common language or nomenclature. With no standard practice for reporting, it is much more difficult to share and integrate data. *“This issue of sharing data elements comes up specifically in the context of the nomenclature of the genomic reporting because part of the complexity comes from the lack of a standard. Everybody reports differently. Some people report at a gene level, and genes aren’t even always called the same thing. Some report at the variant level. Some report out nucleotide change. Some report an amino acid change,”* said one participant. Payers, regulators, and clinicians agreed that at a minimum it would be worthwhile for the leaders of each study to share the data elements being used to report the genomics. One study designer asked, *“Could we converge on a standard report format; could we figure out a way of mapping across the different elements that people may choose to use?”*

What to standardize?

Led by a regulator, several stakeholders supported a *“move towards standardizing data inputs and outputs for these studies as the low-hanging fruit.”* Data standardization was viewed as a prerequisite for meaningful aggregation and subsequent analysis of the data. Many members of the group wondered whether the FDA could leverage its stature and promote standards, similar to what it has done in the past. However questions remain as to what information requires standardization: *“It’s great to standardize actionable mutations coming from all these efforts, but also why not get all the data? I mean ultimately ideally it would be whole-genome sequencing data, and that’s a big data effort. But I think that is where we really need to go.”* A lab director added, *“At the very least there should be a minimum, a set of genes that we are testing, so at least there is something when we aggregate the data that we can actually pull together.”*

The importance of leadership and incentives

An HIT leader observed that the challenges of data collection and sharing, integrating genomic and clinical information, and creating feedback mechanisms in service to continuous learning *“are not technology problems. The technology already exists to address these issues. The issue here is more one of leadership and competing incentives. We’re siloed in how we work and how we are incented. To solve this problem, we need greater alignment.”* Recognizing the work to be done, another industry leader added, *“Who*

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should and can step up? Who is willing to deal with the practical implications of providing integrated solutions – to address costs and the need for new business models?”

Several payers, oncologists, and industry leaders suggested the NCI “step up and assume a leadership role on this data-sharing agenda for genomics-driven real-world studies,” but others questioned whether the NCI would be interested in assuming a leadership role on these issues, with one oncologist lamenting, “The NCI seems to be a natural leader for this kind of work. A government actor can be a neutral third party whose mission is to act in the best interest of the public. They could be influential in setting data standards, yet it seems like they do not want to engage.” Some suggested that the group look to academic centers to take on a leadership role, but others raised an incentive challenge: “A lot of academic centers are looking at their data as a commodity, and with decreasing costs, they are saying, ‘We want to use this as a commodity and can’t give data away for free.’” A lab director added, “Everybody thinks they will be able to monetize their data set. Well, it is interesting that every lab is collecting data to monetize, which means we have a lot of sellers, no buyers, and several missed opportunities to pool evidence.”

Progress on oncology outcomes

With the goal of improving health outcomes and patient benefits in mind, the HIT representatives advised the group to step back from a genomics-focused agenda and consider a broader systemic approach. They asked if a multistakeholder group could consider the integration of genomic information with other types of data that accrue around a patient over the course of clinical care.

An HIT representative commented, “Achieving improved patient benefit and health outcomes may require greater uptake of genomic tools, but will likely require a more integrated model that considers stakeholder incentives, data collection in the clinic and at home, physician education, and behavior modification.” A payer added, “We are entering a world where outcomes are ruling the day. Yes, it is important to think about specific tools like NGS, but it is just as important to think about the rest of the care pathway and the cost of additional interventions. At the end of the day, each of us will have to work together in a different way to deliver an outcome, not an input.” A healthcare leader encouraged the group to imagine a system of care characterized by the most accurate, valuable clinical management, in which information is fed back to carefully curated studies.

In an effort to assume a more holistic approach to oncology care that includes but is not limited to genomics, an oncologist asked the group whether there were ways to ensure genomic data flows into the EMRs. “Right now the reporting is basically done through separate mechanisms. The only way anything gets into an EMR is by scanning a PDF. It’s not queryable. It’s not workable ... If the test generators could get comfortable with and develop mechanisms to report results directly into the EMR, then when you query the EMR for the outcome data, you can also query it for the genomic data.”

One HIT leader reminded other participants, “If structured genomic data becomes a part of the EMR, it must be objective, it must be searchable ... Not only the data that’s come out of the analysis, but also the data that can be used to identify outcomes, progress, issues, [and] side effects, needs rules on reporting standards. We need a shared language if we want to integrate this data into the actual clinical experience.”



The necessity of new models of leadership and collaboration

A majority of participants declared their commitment to carry this discussion forward in a collaborative fashion. A payer challenged the group *“to leverage these studies for greater societal good. As we continue to consider the patient as the center of this universe, I hope that we come to the conclusion that although competition may be good, collaboration may well be better.”* Participants identified several “quick wins” that a multistakeholder group might undertake:

Create an index for genomics-driven/observational studies

Several stakeholders lamented the inability to *“go to one place and see the range of studies being conducted with NGS in the real-world setting.”* A clinician proposed the creation of a study index that would make it easier to align patients to real-world genomics studies. *“One really good goal we could hope to achieve is to figure out a strategy to be able to navigate patients to the right study so that the studies can accrue optimally, and every patient who could potentially participate in a study gets the opportunity to do that.”*

Convene a data-sharing working group

Given participants’ interest in sharing data more readily, one payer proposed creating a working group focused on identifying common data elements, methodology, and study objectives across a sample of genomics-driven observational studies. A disinterested third party could serve as counselor, referee, and aggregator. *“It can be somebody from Philips or GE or somebody around the table who understands HIT and genomics but doesn’t get hung up in the weeds about whether something is actionable or not,”* suggested a payer.

Participants in this group would determine the circumstances under which data should be shared. They would list and share all of the data elements they are collecting and would agree on a minimum core set of elements before launching into a data-sharing discussion. *“Make sure that everybody is collecting a certain minimum data set, and then whatever else you want to collect that serves the needs of your particular study, you should of course collect. But before we actually try to share any data, let’s share all the data elements so that we all have a clear understanding of what each effort is collecting, and then we can have something to build upon,”* said a physician who engages in research.

One of the most important issues this working group could tackle would be the harmonization of data standards in three domains: data inputs, IT system/technical specifications, and data outputs. A regulator suggested, *“At the very least, a group like this should standardize nomenclature for data outputs such that they are fit for purpose for the broadest-use case, something that would apply to the broadest group of stakeholders.”* Payers agreed that achieving consensus on data harmonization would be a useful path forward: *“There is definitely inherent value if the leaders of these studies could work together and identify minimum data elements to collect. Maybe it is as simple as saying, ‘We’ll collect clinical data, how treatment was delivered, and what the outcome was.’ Once you’ve done this, maybe you can commit to data sharing and transparency.”*



Reevaluate meaningful-use criteria

A regulator raised the possibility of the group's helping to reevaluate the meaningful-use criteria.¹⁵ He asked, *“What additional information could we integrate into the EMR in a structured fashion? What’s not digitized right now? Mutations, path reports, staging information? All of this could be integrated into the meaningful-use criteria.”* Several oncologists welcomed the idea, with one stating, *“I think we’ve reached a point where we have to reevaluate the meaningful-use criteria, and I think this is a great opportunity to do that in a multistakeholder kind of fashion. Right now there are some simple cancer-related outcomes that are almost impossible to extract from EMRs. If we truly want the ability to mine genomic and clinical data in one swoop, this would be a great first step.”* Another added, *“Let’s scrap the ‘meaningless-use’ criteria that we have now, and let’s put in ... two meaningful-use criteria. You must put in the stage of the cancer, so you have the staging information in there, and you must put in what the response to treatment was in some structured format. And if we just had those two things [along with the genomic data], we’d have a lot more useful information that we could extract from EMRs for cancer patients.”*

Convene a regulatory-focused group to define real-world evidentiary standards

An industry leader proposed convening a small focus group comprising the FDA, potentially also the European Medicines Agency, payers, and leading registry innovators to discuss the level of evidence, scope of metrics, and quality requirements needed to use registry data for subsequent regulatory benefit. One industry leader summarized: *“A good outcome from this meeting would be a focused multistakeholder discussion with the FDA about what they need to see from any of these studies in order for the data to have regulatory value.”* A clinician said that outcomes from such a group could inform subsequent guidance from the FDA: *“The FDA could take the inputs from the [proposed group] and issue a public statement through a draft guidance mechanism on the data set characteristics from observational studies needed to support regulatory decisions.”* Another clinician suggested the FDA provide explicit guidance on consents, quality control, data elements, and additional information on how researchers should construct registries. A regulator agreed that the proposed approach has value, noting that at a minimum, a *“white paper on norms and standards for real-world registry reporting and the nomenclature for evidentiary standards for real-world evidence may be useful.”*

Convene a payer-centric multistakeholder group to discuss evidentiary considerations for these studies

While several meeting participants sought input from the FDA on evidentiary standards for real-world studies, just as many sought the payer perspective. Noting the impact of clinical utility as a driver for coverage and reimbursement, one HIT leader asked, *“Can we get a few payers to sit down with some of these study investigators for an honest discussion of what data they would like to see? What questions do they want answered? How vast or narrow does the data set need to be?”* A lab director added, *“What*

¹⁵ HealthIT.gov, a US government website on health IT, defines meaningful use as the use of EMR technology to improve quality, safety, efficiency, care coordination, and population and public health, to reduce health disparities, and to engage patients and family while maintaining patients' privacy and the security of patient information. The site adds that the goals of meaningful-use compliance are better clinical outcomes, improved population health outcomes, increased transparency and efficiency, empowered individuals, and more robust research data on health systems. See [“Meaningful Use Definition and Objectives.”](#) HealthIT.gov, February 6, 2015.

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outcomes are [payers] OK with? Would three or four case reports be enough? Do you really want a TAPUR or MED-C model to generate the data, or is there a simpler path? Can we put a proposal before you and see if addresses your concerns?"

An oncologist called on the payers to lead this effort, given that *"they are the biggest beneficiaries of these registries. These studies will give them a lot of data on what does not work and what they will no longer have to pay for."* Some payers acknowledged a benefit but said that other stakeholders, such as pharma, were the primary beneficiaries. Still, some payers appeared interested in such a discussion, with one exclaiming, *"We don't have to just burrow into clinical-utility conversations. Of course we have to ask 'How can a health plan facilitate the accumulation of knowledge that will improve care?' But yes, there's certainly a role we can play in that dialogue."*

Convene a group to discuss and develop business models to support these initiatives over the long haul

Participants acknowledged the cost of running registries, collecting data, and building the infrastructure to share data and integrate genomic and clinical information. They understand the start-up cost and the price of sustaining these efforts. However, a number of participants identified a tension between those interested in generating the capital required to sustain a study and those focused on profit-driven solutions. Several suggested the group spend more time discussing alternative financial models to support these efforts. A health system leader commented, *"The business challenge is a real one. 'Commercial' isn't a bad word. We just need to decide what we need money for and where do we want to assign a price tag for profit?"* A researcher added, *"There's fundraising to jump-start a study, there's monetizing data for a profit, and there's an option to make data freely available and monetize the analysis or 'healthcare solutions' you derive from that data. I could envision a group digging into all of these issues."*

Conclusion

Participants affirmed the interest and action focused on the capture of genomics and outcomes data, both from rigorously scoped clinical trials and in real-world cancer treatment. At present, however, there is no single evidence-based model or blueprint to instruct healthcare leaders on how to use genomics and outcomes data to achieve positive health outcomes for patients, health systems, and society. Healthcare leaders will need to experiment with various demonstration projects and new models to identify the best path forward. Oncology presents a vast area for such experimentation, as evidenced by the new trials and registries that continue to emerge. To contribute in a meaningful way, these and future studies will require continuous learning, clear evaluation, open governance, and an appropriate culture and infrastructure to support them.

The oncology summit provided a starting point for defining the areas of challenge and potential approaches/pilot areas for moving forward. This forum also established a nucleus of committed healthcare leaders willing to move beyond siloes and toward collective progress on improving outcomes for patients. A clinician summarized, *"While there is much to do to create a continuous learning system for healthcare that*

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benefits patients and improves outcomes, strengthens clinical care, sustains innovation and is cost-effective, I am heartened by the commitment of the leaders around this table to work together and make it happen.”

About this document

The views expressed in this document represent those of the Sustainable Predictive Oncology Therapeutics and Diagnostics (SPOT/Dx) Working Group, a group of leading stakeholders from the public and private sectors committed to improving patient outcomes by equipping US healthcare leaders with the tools needed to change the diagnosis and treatment of cancer. This document is not intended to represent the particular policies or positions of the Working Group’s individual participants or their affiliated organizations. This material is prepared and copyrighted by Tapestry Networks with all rights reserved. It may be reproduced and redistributed, but only in its entirety, including all copyright and trademark legends. Tapestry Networks and the associated logo are trademarks of Tapestry Networks, Inc.

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Appendix A: Invited Participants

Patient/policy advocates

- Jeff Allen, Executive Director, Friends of Cancer Research
- Nancy Roach, Founder and Chairman, Fight Colorectal Cancer

Payers

- Naomi Aronson, Executive Director, Clinical Evaluation, Innovation and Policy, Blue Cross and Blue Shield Association
- Mike Barlow, Vice President, Operations, Palmetto GBA
- Joseph Chin, Acting Deputy Director, Coverage and Analysis Group, Centers for Medicare and Medicaid Services
- Michael Kolodziej, National Medical Director, Oncology Solutions, Aetna
- Robert McDonough, Head of Clinical Policy Research and Development, Aetna
- Lee Newcomer, Senior Vice President, Oncology, Genetics and Women's Health, UnitedHealthcare
- Girish Putcha, Director of Laboratory Science, Palmetto GBA
- James Rollins, Director, Coverage and Analysis Group, Division of Items and Devices, Standards and Quality, Centers for Medicare and Medicaid Services
- Alan Rosenberg, MD, Vice President, Medical and Clinical Pharmacy Policy, Anthem
- Deborah Smith, Managing Director for Medical Policy for the Federal Employees Program, Blue Cross and Blue Shield Association
- John Yao, Staff Vice President of Medical Policy and Technology Assessment, Anthem

Regulators

- Bob Becker, Chief Medical Officer, FDA – Center for Devices and Radiologic Health (CDRH)/Office of In Vitro Diagnostics and Radiological Health
- Gideon Blumenthal, Clinical Team Leader, Thoracic and Head/Neck Oncology, FDA
- Sean Khozin, Senior Medical Officer, FDA – Office of Hematology and Oncology Products
- Christopher Leptak, Office of New Drugs (OND), Biomarker Lead, FDA – Center for Drug Evaluation and Research (CDER)
- David Litwack, Personalized Medicine Staff, Office of In Vitro Diagnostics and Radiological Health, FDA – CDRH
- Elizabeth Mansfield, Associate Director for Clinical Studies, Personalized Medicine, FDA
- Michael Pacanowski, Associate Director, Genomics and Targeted Therapy, Office of Clinical Pharmacology, Office of Translational Sciences, FDA – CDER
- Francesco Pignatti, Head Oncology Evaluation, European Medicines Agency
- Rick Pazdur, Director of the Office of Oncology Drug Products, FDA

Subject matter experts/technology specialists

- Steve Anderson, Global Head, Clinical Trials; Chief Scientific Officer, Oncology and Genetics, LabCorp Clinical Trials
- Barbara Conley, Associate Director, Cancer Diagnosis Program, NCI-MATCH

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- Bill Dalton, Founder and Chief Executive Officer, M2Gen
- Dane Dickson, CEO, MED-C
- Andy Faucett, Director of Policy & Education, Office of the Chief Scientific Officer, Geisinger
- Christopher Fikry, Vice President, Oncology at Quest Diagnostics
- Keith Flaherty, Director, Henri and Belinda Termeer Center for Targeted Therapy, MGH
- Jason Gillman, Director, Precision Genomics, Intermountain Healthcare
- Vassilis Golfinopoulos, Medical Vice Director, EORTC
- Dan Hayes, President-Elect, American Society of Clinical Oncology
- Lee Hilborne, Senior Medical Director, Medical Affairs (CPT Coding and Advocacy), Corporate Medical Director, Clinical Pathology, Quest Diagnostics
- Jon Hirsch, Founder and President, Syapse
- Patrick James, MD, Chief Clinical Officer, Health Plans and Policy, Medical Affairs, Quest Diagnostics
- David Ledbetter, Executive Vice President and Chief Scientific Officer, Geisinger
- Gary Palmer, CMO, NantHealth
- John Pfeifer, Vice Chair for Clinical Affairs, Pathology and Immunology, Washington University School of Medicine
- Richard Schilsky, Chief Medical Officer, American Society of Clinical Oncology
- Randy Scott, Cofounder and CEO, Invitae
- Gary Stone, Operations Officer, Administrator, Precision Genomics, Intermountain Healthcare
- Mickey Williams, PhD, Director, Molecular Characterization Laboratory, Frederick National Laboratory for Cancer Research

Sponsor representatives

- Ken Bloom, Chief Medical Officer, GE Healthcare – Clariant Diagnostic Services
- Jeff Caron, Chief Software Architect, Software Technology Office at GE Healthcare
- Cindy Collins, Chief Executive Officer, In Vitro Diagnostics and Research & Applied Markets, GE Healthcare
- Howard Fingert, Senior Medical Director, Takeda Pharmaceutical Company
- Hans Hofstraat, VP, Philips Research
- Robert Loberg, Director, Medical Sciences and Therapeutic Area Lead, Clinical Biomarkers, Oncology, Amgen
- Bob Reese, Senior Vice President and Global Partner, Philips
- Helen Routh, Senior Vice President, Strategy & Innovation, Philips
- Maria Trolliet, Senior Manager, Global Regulatory Affairs Development, Takeda Pharmaceutical Company