How Lean Methodology Can Improve Molecular Testing Processes in Advanced NSCLC

BY LAWRENCE D. WAGMAN, MD, FACS; RAYMOND CASCIARI, MD; JOHN MAURICE, MD; PEGGY J. CRABTREE, MBA, RN; AND RUSLAN HORBLYUK, PHD, MBA

The demand for molecular testing services has grown at an enormous rate in recent years, as molecularly-targeted therapies have revolutionized the approach to cancer treatment and challenged the ability of molecular testing facilities to keep pace.[1] In addition, the efficiency of molecular testing processes is increasingly becoming an operational concern for healthcare providers as it relates to the initiation of therapy and in the cost-containment environment driven by reduced reimbursement.[2] Targeted therapies with molecular testing requirements are a prime example of processes that contain natural gatekeepers in their operational flow. Process improvement techniques can help identify the underlying inefficiencies that are delaying or deterring patients from receiving treatment they require.

An example of such a process improvement technique is "lean" methodology, which was developed by Toyota to improve flow and minimize waste.[3,4] In the healthcare setting, lean methodology aims to maximize value to the customer—typically patients—while minimizing any activity that is not valued (i.e., "waste") to provide a streamlined, valued-added service through five simple principles:[3,4]

1. Identify the value
2. Map the value stream and identify waste
3. Create a constant flow of value and eliminate waste
4. Pull patients along their journey
5. Aim to continually improve the patient journey.

Although lean methodology has only been applied in the healthcare industry for a decade, its tools have been used in manufacturing and other industries for more than a century. Clinical laboratories began adopting lean methodology some time ago, resulting in improved turnaround time and workflow, despite high test volumes.[5]

In U.S. healthcare systems, interest in the use of lean process improvement has increased since the passage of the Affordable Care Act (ACA).[6,7] Healthcare providers, payers, and pharmaceutical companies alike are tasked with finding opportunities to reduce cost, improve efficiency, reduce waste, and improve the patient experience at all levels of their organizations—with the ultimate aim of reducing the national expenditure on healthcare and maintaining quality measures. Implementation of lean interventions has the potential to reduce the cost of services incurred by providers and to improve the timeliness of treatment initiation.[5] For example, use of lean methodology in the design of new clinics has been found to improve patient volume, lead time, and satisfaction, while reducing operating costs.[7]

> ...the efficiency of molecular testing processes is increasingly becoming an operational concern for healthcare providers...

Current clinical guidelines in lung cancer treatment recommend that molecular testing results be available within 10 working days of receipt of tissue.[8] Some of the focus that has been given to developing the molecular tests themselves must now turn to improving performance on the front end of the molecular diagnostic testing cycle, from when patients first enter the provider setting and throughout the remainder of their care journey.

Lean in Practice: A Pilot Study

To see how lean methodology could be used to evaluate current molecular testing processes, identify waste, and design an improved process for advanced non-small cell lung cancer (NSCLC) in the community setting, a pilot study was conducted at St. Joseph Hospital, Orange, Center for Cancer Prevention and Treatment (SJH), located in Orange County, Calif. The study also evaluated the applicability of any improved processes to other disease sites within the organization and to the St. Joseph Health System as a whole. The study focused on NSCLC adenocarcinoma (which accounts for about 40 percent of all NSCLC cases),[9] for which two targeted therapies were available at the time the study was conducted: erlotinib for patients with epidermal growth factor receptor (*EGFR*) mutation and crizotinib for patients with anaplastic lymphoma kinase (*ALK*) gene rearrangement and metastatic disease. These actionable mutations occur in relatively small

numbers of patients; *EGFR* mutations are estimated to occur in 10 to 15 percent of Caucasian patients and 40 percent of Asian patients with adenocarcinoma and *ALK* rearrangement in 2 to 7 percent of all patients.[10] These percentages raised the question of how the common bottlenecks and barriers that exist in a tertiary community cancer center impact the ability of clinicians to achieve optimal efficacy in identifying a small number of patients for potential targeted treatment.

> ...applying lean methodology could streamline the care process and ultimately create value for patients through a more timely and protocol-driven molecular testing process...

SJH is a National Cancer Institute (NCI)-designated Community Cancer Center at which an estimated six to eight new cases of NSCLC are treated each month. Within SJH's Thoracic Oncology Program, a comprehensive multidisciplinary team is dedicated to patient care. Supplementing the traditional physician team (medical oncologists, pathologists, pulmonologists, radiologists, radiation oncologists, and thoracic surgeons) are nurse navigators, genetic counselors, registered dietitians, social workers, pain managers, and other nursing and radiology staff. The Thoracic Oncology Program also offers other services, such as computed tomography (CT) screening, video- and robotic-assisted thoracic surgery, radiofrequency ablation, high-dose-rate brachytherapy, pulmonary rehabilitation, an outpatient infusion center, a lung cancer support group, and smoking cessation classes, as well as access to clinical trials to stay at the leading edge of research and innovation. Moreover, SJH is considered a lean organization, and many of its leaders have been trained in lean techniques.

Within the pilot study, the patient journey focused on the subset of patients diagnosed with biopsy-confirmed NSCLC adenocarcinoma of stage IIIb or higher who underwent molecular testing and ultimately received targeted treatment. (Per National Comprehensive Cancer Network [NCCN] guidelines prior to 2014, NSCLC adenocarcinoma of stage IIIb or higher was eligible for molecular testing; 2014 NCCN guidelines recommend that only stage IV tumors be tested.[11]) Researchers involved in the SJH pilot study hypothesized that applying lean methodology could streamline the care process and ultimately create value for patients through a more timely and protocol-driven molecular testing process by eliminating or reducing existing process inefficiencies.

Mapping the Value Stream

Within the SJH pilot study, the key lean principle used was a value stream map (VSM) to assess the current state and design the ideal future state of the care process. To better visualize the processes, progression, waste, and value, the researchers developed an innovative "hybrid value stream map" that combined traditional process mapping tools and lean VSM components.

Researchers conducted semi-structured one-on-one interviews with stakeholders about the current state of the care process and the physician experience at SJH. Group consensus about the current state map was reached with the dedicated multidisciplinary team through the use of lean tools and process mapping. Researchers then worked with the team members to develop the future-state molecular testing process and metrics to support this process. The researchers and selected physician leaders devised an action plan for implementing the monitoring of the metrics, developing a molecular testing protocol, and finalizing the future-state process map.

Major themes of the interviews included:

- Utilization of the molecular testing process
- Tissue insufficiency post-biopsy
- Patient experience
- Utilization of guidelines and protocols
- Communication across the care team
- Reference lab processes
- Reimbursement and cost
- Overall efficiency of the care process.

The interviews showed that the existing protocols for initiating molecular testing at SJH were being used inconsistently, with a high degree of variability that was mostly due to differing perspectives on when reflex testing should be done. Multidisciplinary team members who were aware of the protocol recognized that it was used on a limited basis. Perceived delays in obtaining authorizations for molecular testing and insufficient quantities of tissue were all cited as reasons for further testing delays. Indeed, in some cases it was not apparent from whom authorization should be sought. The interviews also identified the challenges associated with the hospital resources responsible for data collection at the center. Previously, data collection had focused on diagnostics, cancer volumes, and treatments delivered, including cancer registry metrics. Under healthcare reform, however, data collection must now include data to monitor patient experience, access, outcomes, and patient throughput in order to demonstrate value. At the same time that the pilot project was being conducted, simultaneous development of a centralized process within the St. Joseph Health System also improved the accession of these data.

Evaluating the Current State of the Care Process

The next stage of lean implementation was a two-hour session between researchers and the multidisciplinary team to evaluate the current state of the care process, in order to understand all the processes, inputs, outputs, and suppliers and lay them out visually in a hybrid value stream map. Five key components of the care process were built into the framework:

1. ***Patient access:*** all areas through which the patient enters the process (e.g., the hospital or an outpatient setting) and diagnostic testing
2. ***Tissue collection:*** the various points and providers responsible for the biopsy
3. ***Histologic diagnosis:*** evaluation of biopsy tissue by the pathology team for definitive diagnosis and adequacy of tissue for further studies
4. ***Clinical and molecular diagnosis:*** assessment by the oncology team of the pathology diagnoses and determination of appropriate care, including the need for molecular testing
5. ***Treatment:*** determination by the medical oncologist and multidisciplinary team of the most appropriate course of treatment (targeted therapy, chemotherapy, or other).

Several waste elements were identified and highlighted within the hybrid value stream map (see Figure 1, pages 38-39). There was group consensus on the need for primary care physician (PCP) education on patient flow with regard to molecular testing, as well as on lung cancer as a whole. Suggestions included raising PCP awareness that SJH offers molecular testing to better identify and treat advance-stage cancers, that a lung cancer diagnosis is not always fatal, and that referral pathways do exist. In turn, education could lead to wider support among PCPs for lung cancer screening to aid early detection. However, the key to reaching PCPs may be through patient education and social media to prompt patients to initiate discussion and question their PCPs.

Another potential area of waste was the approval process for biomarker testing in the various payer venues, including managed-care, commercial, low-income third-party, and traditional Medicare. The anxiety over possible front-end delays in the process with multiple types of health insurance, each with unique and occasionally arcane regulations, was emphasized. However, the medical oncologists who typically submit the authorizations differed widely in their view of this process and its impact as a barrier in the molecular testing process.

There was significant focus on clinical processes for obtaining appropriate tissue quantity and quality during biopsy. Given the past struggles with quantity and/or quality not being sufficient (QNS) for molecular and other testing, the thoracic oncology team had already moved away from fine-needle aspiration and begun focusing more on core-needle biopsies. Despite this, the interviews indicated that up to 40 percent of samples are QNS for molecular testing, frequently requiring re-biopsy that resulted in a delay in treatment. The current-state discussions again highlighted uncertainty among members of the multidisciplinary team as to whether the oncologist or pathologist was responsible for ordering molecular testing when clinical history and histologic diagnosis confirms a "known" stage IV NSCLC. This led to high variability and process waste in practice and execution.

Another identified area of waste was developing the packet of information on patients referred into SJH during their biomarker evaluation process journey. Although referrals from PCPs or non-specialists to specialists are standard practice, gathering the requisite information (medical history, imaging studies, histologic diagnosis, remaining tissue, consultations with specialists) typically created a bottleneck. In order for the multidisciplinary team to provide the referred patient with the highest quality care, a number of authorizations, medical history reviews, and course of action reviews were required before an appropriate treatment plan could be implemented.

There were also functional delays in identifying, screening, and accruing patients for clinical trial research. The current infrastructure for patient data mining was cumbersome due to the de-centralization of the data sources, thereby causing delays in enrolling patients in appropriate clinical trials at the time of histologic diagnosis. Operational delays as simple as office hours, clinical trial biopsy requirement, and patient access to the informed-consent process exacerbated the delays.

Lastly, timeliness of cross-functional communication across the multidisciplinary team members was identified as an overarching area for improvement throughout the care process.

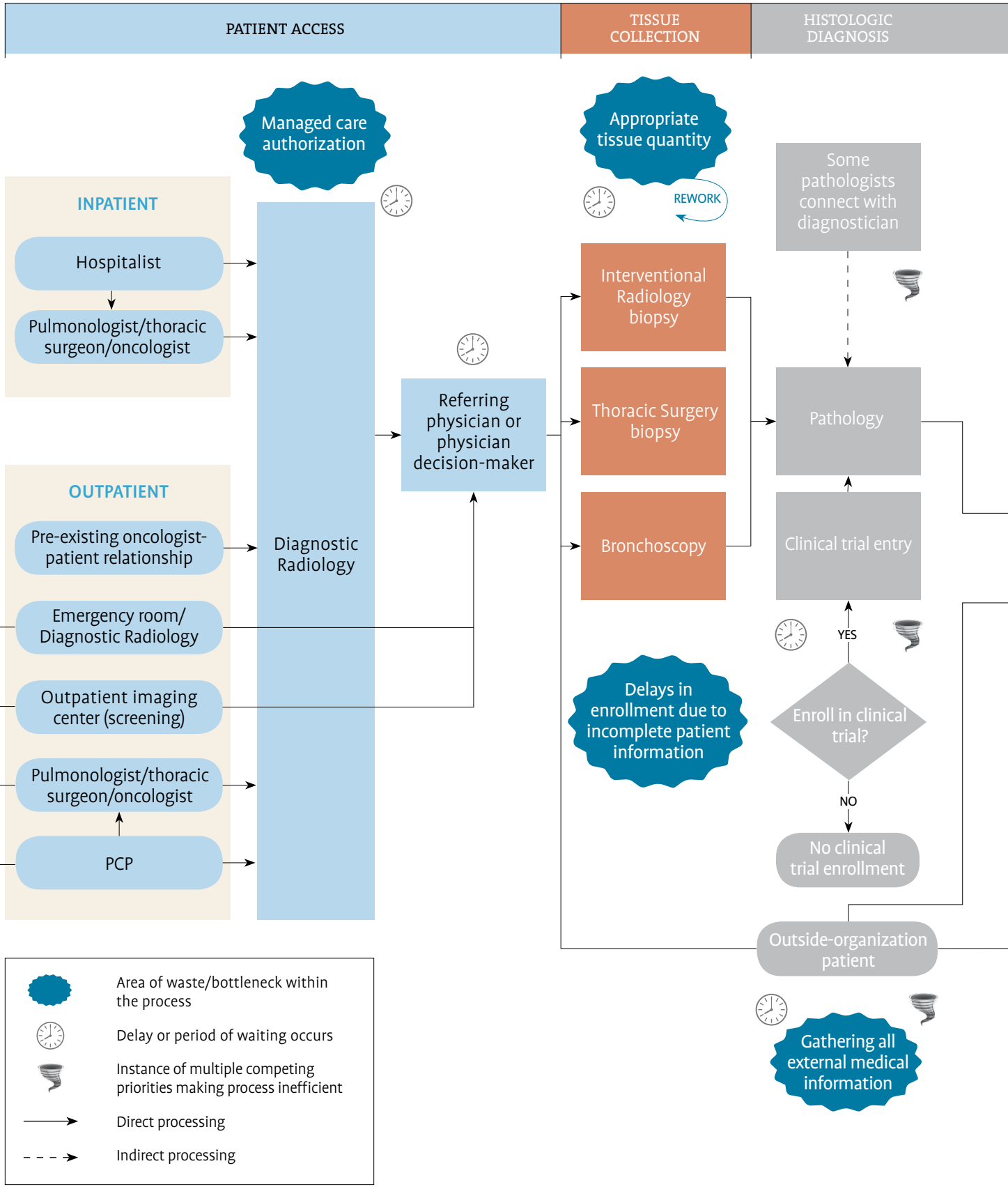
Determining the Ideal Future State of the Care Process

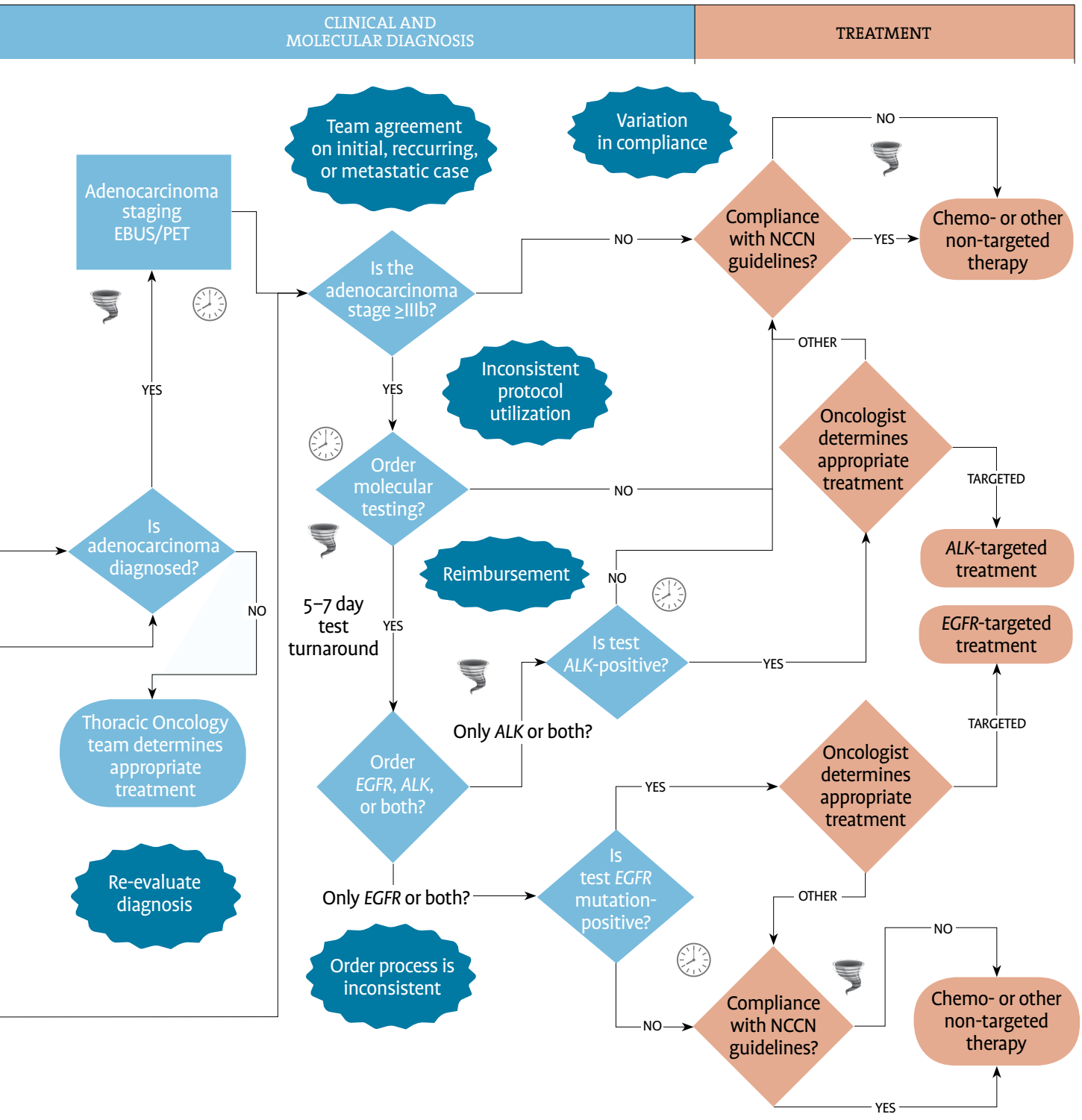
Upon consideration of the current state, physician leaders highlighted that the strength of SJH's thoracic oncology team was its use of a multidisciplinary conference that meets weekly to discuss specific oncology cases. (About 45 members of the multidisciplinary team, including pulmonologists, pathologists, radiation oncologists, medical oncologists, thoracic surgeons, interventional radiologists, and nurse navigators attend these conferences.) The physician leadership viewed this process improvement as a baseline for developing a streamlined blueprint for future innovations and developments within a new, value-added process that could be scaled up to include other sites (e.g., breast or colorectal cancer) within SJH. Additionally, best practices could be provided to other cancer centers.

Walking through the different components of the care process, the team modified pathways to eliminate barriers, areas of confusion, duplicate processes, and areas of rework to assure a streamlined future state that provides optimal value to patients

(continued on page 42)

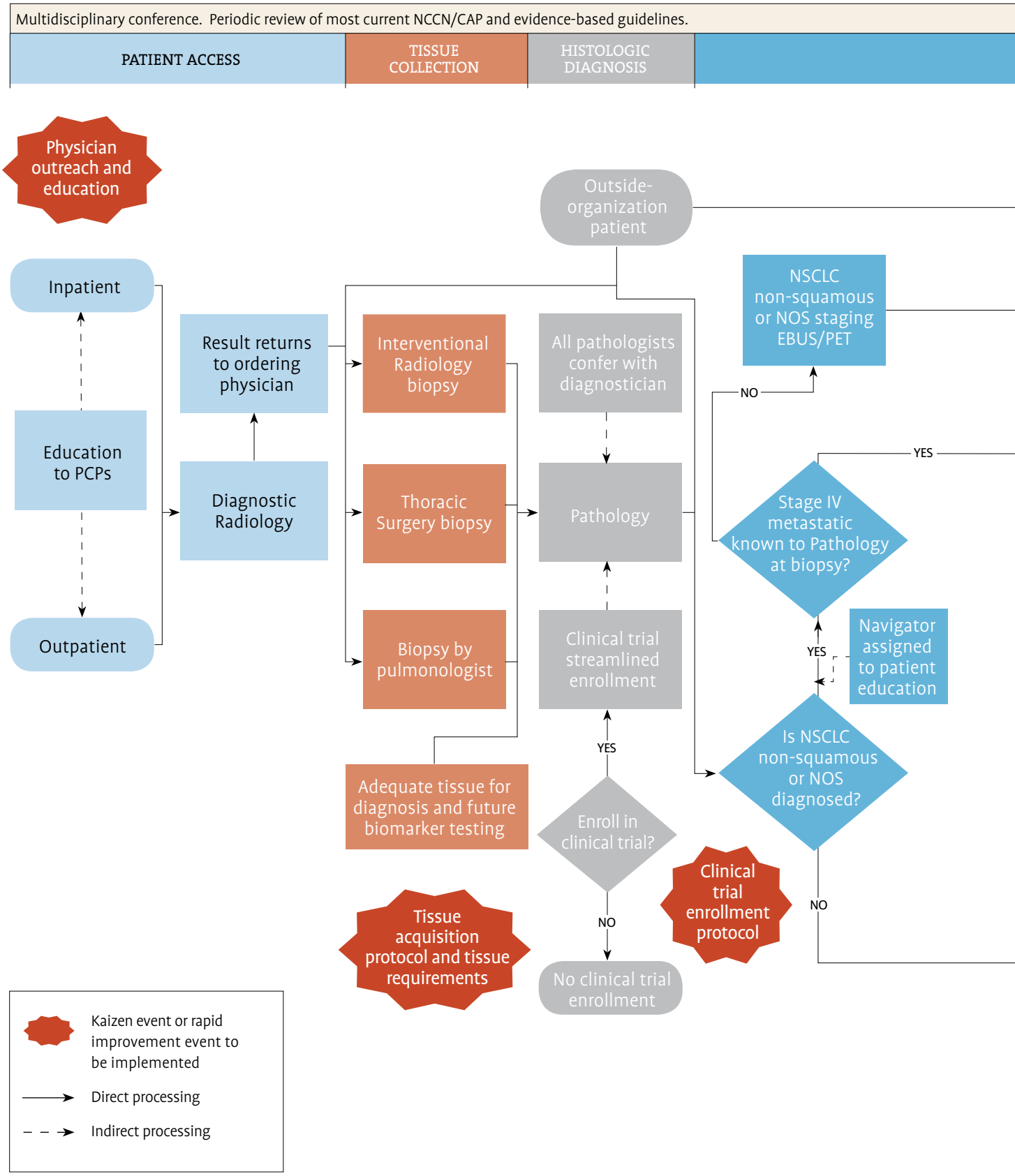
Figure 1. Hybrid Value Stream Map for the Current State of the Care Process

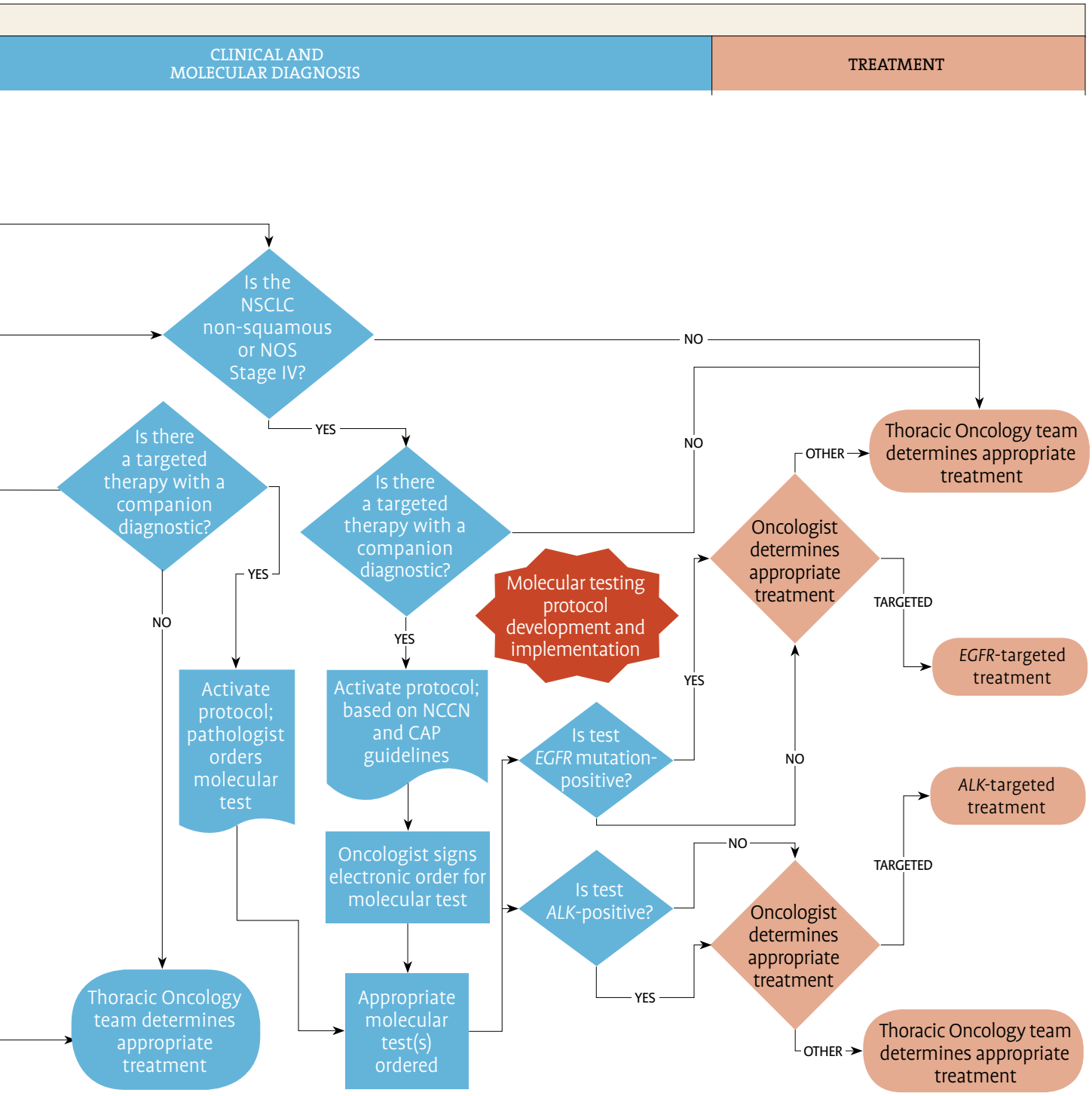




Glossary. *ALK*: anaplastic lymphoma kinase; EBUS: endobronchial ultrasound; *EGFR*: epidermal growth factor receptor; NCCN: National Comprehensive Cancer Network; PCP: primary care provider; PET: positron emission tomography.

Figure 2. Hybrid Value Stream Map for the Ideal Future State of the Care Process





Glossary. *ALK*: anaplastic lymphoma kinase; CAP: College of American Pathologists; EBUS: endobronchial ultrasound; *EGFR*: epidermal growth factor receptor; NCCN: National Comprehensive Cancer Network; NSCLC: non-small cell lung cancer; NOS: not otherwise specified; PCP: primary care provider; PET: positron emission tomography.

(continued from page 37)

Table 1. Action-Oriented Rapid Improvement Events

Physician Outreach and Education

- Town hall meetings with PCPs to discuss thoracic oncology issues
- Inclusion of select PCPs in multidisciplinary thoracic oncology meetings
- One-on-one educational sessions with PCPs on thoracic oncology treatment options and use of molecular testing

Tissue Acquisition Protocol and Tissue Requirements

- Assigning criteria for tissue sample extraction by modality (i.e., needle size, biopsy extraction method, etc.)
- Defining specific minimal biopsy tissue requirements that are sufficient for testing but also patient- and system-friendly

Molecular Testing Protocol Development and Implementation

- Protocol for the responsibilities of ordering molecular testing through use of future-state process criteria (pathologist or oncologist)
- Protocol compliance tracking
- Development of automatic triggers for testing based on clinical status

and stakeholders (see Figure 2, page 40-41). The team outlined three key action-oriented events (in lean terms, "kaizens") to rapidly address areas of inefficiency (see Table 1, above). Participants also agreed that information-sharing stages within the multidisciplinary team, as well as with other program leaders and the SJH administration, should be incorporated throughout the care process.

Two subsequent meetings were held with the multidisciplinary team to review and finalize potential metrics for tracking the adoption of the future state by the SJH Thoracic Oncology Program and to assure the long-term sustainability of the initiative. In the first meeting, participants brainstormed metrics that could be tracked within SJH's current data infrastructure. Among the metrics suggested were variability of cycle times, biopsy QNS rate, cost impact, patient treatment preferences, and protocol compliance.

The study sponsors (the cancer center director, the chief medical officer, and the Thoracic Oncology Program director) were then tasked with selecting the top six metrics to be implemented in the pilot.

In the second meeting these metrics were revisited, and consensus was reached on the final list of metrics:

1. Re-biopsy rates
2. Percent of patients tested with biomarkers who received targeted therapy
3. Number or percent of patients with adequate tissue at time of biopsy to complete biomarker testing
4. Percent of various techniques yielding adequate tissue
5. Aggregated cost of performing test (i.e., scheduling, biopsy, procedure, pathology)
6. Measurement of adherence to protocol
7. Cycle time (time from biopsy order to receipt of results).

Once the metrics were finalized, the participants tasked a work group with determining the granular components needed to support the metrics and assigning accountability for implementation. The stakeholder departments involved in this ongoing implementation effort are the cancer registry, decision support, information technology, quality, and cancer center medical and administrative leadership.

Future Steps

The SJH pilot study successfully employed lean methodology and identified areas of improvement for the molecular testing process in a subgroup of patients with advanced NSCLC. Program evaluation is underway to quantify the impact of this initiative. Through active buy-in of leadership into the pilot process and ongoing engagement through the challenges of transition to the future-state design, the potential for improved efficiency and

Disclosures

Lawrence D. Wagman, Raymond Casciari, and John Maurice have no conflicts of interest to disclose. Peggy Crabtree is an employee of The Camden Group, which received financial support from Pfizer in connection with the development of this manuscript. Ruslan Horblyuk is an employee of Pfizer and holds Pfizer stock.

Acknowledgments

This study was sponsored by Pfizer Inc. Editorial support was provided by Alan Pedder and Wendy Sacks at ACUMED (Tytherington, UK, and New York, NY) and was funded by Pfizer Inc.

The SJH pilot study successfully employed lean methodology and identified areas of improvement for the molecular testing process in a subgroup of patients with advanced NSCLC.

patient access, and reduced operation costs (e.g., re-biopsy, excessive diagnostic testing, professional fees, cost from ineffective pharmaceutical prescriptions, etc.) may be realized. It is anticipated that this will result in improved timeliness, quality of care, and overall patient satisfaction.

The scalability of the pilot study may, however, be limited, as other cancer programs may be structured differently or operate in a different setting (for example, physician group practice versus integrated delivery network), although modular areas within the flow diagram can be swapped in and out to customize for other user groups. Evaluation of the current state revealed that the SJH System is culturally a lean healthcare organization, and was therefore particularly adaptable to implementation of lean methodology. Additional process improvement training may be required in organizations that have not participated in change efforts in the past.

Key to the success of the post-pilot interventions is the presence of committed physician and hospital leadership and the clinical commitment of the multidisciplinary team to ensure compliance. These concepts have already been achieved with NCCN guidelines and evidence-based protocols. Thus, introduction of additional guidelines and locally developed algorithms is likely to be successful. Future evaluation of the qualitative and quantitative impacts of the pilot study interventions and the sustainability of those efforts is recommended. This will, in turn, facilitate the advancement of other technological evolutions, such as single testing, parallel testing, and whole-genome sequencing.[12] OI

Lawrence D. Wagman, MD, FACS, is the executive medical director at SJH and a surgical oncologist with special expertise in cancers of the breast, liver, bile duct, and pancreas. Raymond Casciari, MD, is chief medical officer, the institutional officer for Research, director of the Thoracic Oncology Program, and a certified crew trainer at SJH. John Maurice, MD, is program director of the Thoracic Oncology Program at SJH. Peggy J. Crabtree, MBA, RN, is a vice president with The Camden Group. Ruslan Horblyuk, PhD, MBA, is a director in Outcomes & Evidence, Oncology, Global Health and Value at Pfizer.

References

1. van Krieken JH, Siebers AG, Normanno N. European consensus conference for external quality assessment in molecular pathology. *Ann Oncol*. 2013;24(8):1958-1963.

2. Pasic DM, Samaan S, Yousef GM. Genomic medicine: new frontiers and challenges. *Clin Chem*. 2013;59(1):158-167.

3. NHS Institute for Innovation and Improvement, 2008. Lean. Available online at: www.institute.nhs.uk/quality_and_service_improvement_tools/quality_and_service_improvement_tools/lean.html. Last accessed Nov. 17, 2014.

4. Lean Enterprise Institute. What is Lean? Available online at: www.lean.org/WhatsLean/. Last accessed Nov. 17, 2014.

5. Kibak P. Tools for Benchmarking Performance: How Lean, Six Sigma improve lab efficiency and quality. *Clin Lab News*. 2008; 34(4):1. Available online at: http://old.aacc.org/publications/cln/archive/2008/april/Pages/cover1_0408.aspx#. Accessed August 12, 2014.

6. Grove D. The Affordable Care Act: Shaping Lean Healthcare Facilities Development—Part 1. Healthcare Design; February 2011. Available online at: www.healthcaredesignmagazine.com/article/affordable-care-act-shaping-lean-healthcare-facilities-development-part-1. Last accessed Nov. 17, 2014.

7. Grove D. The Affordable Care Act: Shaping Lean Healthcare Facilities Development—Part 2. Healthcare Design; February 2011. Available online at: www.healthcaredesignmagazine.com/article/affordable-care-act-shaping-lean-healthcare-facilities-development-part-2. Last accessed Nov. 17, 2014.

8. Lindeman NI, Cagle PT, Beasley MB, et al. Molecular testing guideline for selection of lung cancer patients for *EGFR* and *ALK* tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology. *J Mol Diagn*. 2013;15(4):415-453.

9. American Cancer Society, 2014. What is Non-small Cell Lung Cancer? Available online at: www.cancer.org/acs/groups/cid/documents/webcontent/003115-pdf.pdf. Last accessed Nov. 17, 2014.

10. Quest Diagnostics. Lung Cancer Mutation Panel (*EGFR*, KRAS, *ALK*). Available online at: http://questdiagnostics.com/hcp/intguide/jsp/showintguidepage.jsp?fn=Lung/TS_LungCancerMutation_Panel.htm. Last accessed Nov. 17, 2014.

11. National Comprehensive Cancer Network. Non-small cell lung cancer version 4.2014. Available at: www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Last accessed Nov. 17, 2014.

12. Steffen JA, Lentz C. Technological Evolution of Diagnostic Testing in Oncology. *Personalized Medicine*, May 2013.