An Evaluation of the Development and Effectiveness of a Hospital-Based Health Technology Assessment (HB-HTA) Program at the University of Washington Medical Center

Erik J Landaas

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Reading Committee:

Sean D. Sullivan, Chair

Ryan N. Hansen

Geoffrey S. Baird

Program Authorized to Offer Degree:

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University of Washington

Abstract

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Erik J Landaas

Chair of the Supervisory Committee:

Sean D. Sullivan
Dean and Professor
Department of Pharmacy

One of the primary cost drivers for the increase in healthcare costs is new technology, and thirty percent of the overall healthcare spend is from hospitals in the United States. Health technology assessment (HTA) improves new technology adoption decisions by providing a framework within which only those technologies supported by strong evidence are adopted. This dissertation studied the development, implementation and experience of a new hospital-based health technology assessment (HB-HTA) program called Smart Innovation at UW Medicine. Smart Innovation established a formal decision framework including clinicians and executives as well as representatives from supply chain and finance. We describe the methods developed to evaluate new medical technologies, provide the HTA decisions that were made, and report the results of the initiative. In the first two years of the program, we reviewed eleven new technologies and achieved an estimated

$ 5.8 million dollars in potential cost savings/avoidance.

As part of our analysis, we conducted a case study of one HB-HTA, a new molecular test for bladder cancer (Cxbladder) that underwent review by Smart Innovation. The new and less invasive test appeared to be promising, however, there were concerns about its high cost and low specificity. By not covering Cxbladder at UW Medicine, we estimated annual cost savings and avoidance of $1.5 million dollars. The new test was not adopted system-wide; however, a pilot study was conducted to test the diagnostic yield in a narrow patient context. The pilot was a case series that compared two similar groups that were being monitored for recurrent bladder cancer, one that received the new test (Cxbladder) and one that did not. The pilot study evaluated whether the new test changed patient management, and also if the test in question reduced the number of other diagnostic tests ordered.

We also studied the impact of Smart Innovation by comparing technology use at the University of Washington Medical Center (UWMC) to technology use at seventeen similar academic medical centers. The analysis included two technologies, one that underwent Smart Innovation review and one that did not. Specifically, the study compared differences in the number of quarterly surgical procedures and the overall costs between UWMC and control hospitals. Our findings indicated that when UWMC adopted new technologies without HB-HTA review there were no observed differences in utilization compared to control institutions, but when UWMC used HB-HTA methods, there was a reduction in observed utilization and overall costs.

Smart Innovation was successfully implemented at UW Medicine and promoted efficiency in its constituent hospitals. The program reduced costs and utilization, and it also provided a framework under which new technologies of uncertain benefit could be piloted. The

work presented in this dissertation research thus impacted hospital policy and improved UW Medicine's approach to new technology adoption. Smart Innovation started as a pilot program funded by a grant, but following implementation and promising early results, it was incorporated into UW Medicine's Supply Chain Management process. The results of the Cxbladder pilot study likewise changed the institution's clinical practice for ordering the new molecular test for bladder cancer at UW Medicine. Thus, Smart Innovation improved UW Medicine's overall approach to new medical technology review and adoption, as it provided an objective and efficient decision framework and process for reviewing new medical technologies.

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Finally, thanks to my parents, friends and children, especially my wife, Marissa, for her love, patience, and support.

DEDICATION

I dedicate this dissertation research to patients seeking new and curative therapies.

Chapter 1. INTRODUCTION

New technologies are developed by manufacturers, reviewed by regulatory bodies, introduced into the market, and diffused into healthcare systems and settings. Among US hospitals, there are fast and slow adopters and diffusers of new and emerging medical technologies. Among factors responsible for this observation are the levels of sophistication and structures in place to review and make technology adoption decisions.[1]

Hospitals employ a variety of methods and approaches to make new technology adoption decisions, ranging from minimal structures and low evidence requirements to support new technology adoption and diffusion to much more rigorous hospital-based health technology assessment (HB-HTA) programs. Among those without formal Health technology assessment (HTA) programs, there are different approaches to adoption, sometimes limited to financial impact analyses or reviews of patient safety.[2]

This dissertation research studies the experience of implementing a formal HB-HTA program called Smart Innovation at UW Medicine, a large integrated health system in Seattle Washington. Smart Innovation's main objective is to improve technology adoption decision-making within UW Medicine. Smart Innovation operates at the hospital level because in the US, hospitals have become the primary entry point for new technologies and are the single largest cost component of the US healthcare delivery system.[3]

The first aim describes the development of Smart Innovation's decision framework and experience in implementing the new program at UW Medicine. We detailed each new technology adoption decision that was made, as well as reported early fiscal impact results. The second aim was a deep dive into one HB-HTA, a new molecular test for bladder cancer (Cxbladder) that underwent review by Smart Innovation. We had concerns about the new test's high-cost and low

specificity, and our HTA report recommended not covering it. Although the new test was not adopted system-wide, a small pilot study was conducted to evaluate its use in a narrowly-defined clinical context. The pilot study included twelve patients found to have atypical urine cytology with negative cystoscopy and biopsy, of which one group (n=6) received Cxbladder, and one group did not (n=6). The pilot study evaluated whether or not the new test changed patient management. We finally studied the impact of Smart Innovation by comparing University of Washington Medical Center (UWMC) to seventeen similar academic medical centers. The study compared the difference in the number of quarterly surgical procedures and overall costs between UWMC and control hospitals. The analysis focused on utilization of two technologies, one that underwent Smart Innovation review and one that did not.

Chapter 2. DEVELOPING AND INTEGRATING FORMAL TECHNOLOGY ASSESSMENT INTO AN INTEGRATED HEALTHCARE DELIVERY SYSTEM: SMART INNOVATION

2.1 BACKGROUND

New medical technologies are an important part of delivering innovative and cutting-edge health care.[4] They offer hope for improved diagnosis, patient outcomes, curing disease and addressing health problems that lead to chronic illness, disability and low quality of life.[4] The advent of antibiotics systematically improved medicine, saved countless of lives, and changed the leading cause of death from communicable disease to chronic illness in United States (US).[5] However, use of new medical technology is a major contributor to rising costs in healthcare.[6]

When advanced imaging (e.g. computed tomography, magnetic resonance imaging) was introduced it was for specific organs, and the practice expanded to almost every part of the human body, resulting in increased spending.[7] There are also evidence indicating advanced imaging doesn't improve patient outcomes or change clinical care for all areas (e.g. back pain), thereby incurring unnecessary costs.[8] Other elements that impact high cost of new technology include the cost of research and development, patent protection (monopoly pricing), which often lead to higher market prices versus established technologies, and in some cases result in more overall costs when no efficiencies are achieved for the health system.

Sorenson and Drummond summarized eighty-five studies assessing key drivers of medical costs with evidence suggesting that new technologies account for approximately 50% of the growth in healthcare spending in the US and other high-income countries.[6] Their review

indicated new technologies are the largest contributor of increased medical spend when compared to other areas in healthcare such as life expectancy, aging, administration costs, and health care prices. The US Congressional Budget Office (CBO) conducted a study on the fiscal impact of new technology on healthcare spending in the US. The CBO concluded that about half of all growth in health care spending in the past several decades was associated new technology.[9]

Medical costs related to hospitals in the US are the single largest component of the overall US spend in healthcare, accounting for approximately 30%.[3] This has made hospitals a focus for cost-reduction strategies among the Centers for Medicare and Medicaid Services (CMS).[10] Another financial challenge with inpatient hospital reimbursement is diagnostic related groups (DRG) payment systems. DRGs are bundled payment systems that do not account for new and expensive devices, hardware, and diagnostics. Therefore, inpatient care in hospitals is reimbursed based on International Classification of Diseases (ICD) codes and not by line item. Approximately 60-85 percent of total hospital revenues are driven from DRG-based hospital payment systems.[11]

CMS has led efforts to increase the proportion of healthcare being reimbursed by value-based systems, which are designed to incentivize patient outcomes as opposed to fee-for-service arrangements that favor utilization.[10] One of the main drivers that has motivated hospitals to evaluate new medical technologies before they are adopted, is an increased focus on making efficient use of limited resources.[2] Even though this has been an issue over the last few decades, hospitals are increasingly developing hospital level quality and efficiency initiatives based on fiscal efficiency.[12]

Hospital-based health technology assessment (HB-HTA) was developed to improve the decision-making process for adopting new technologies at hospitals.[12] Having a centralized and

rigorous review of new technologies among hospitals prior to adoption is a relatively new phenomenon in the US, but it is becoming more important given payer reimbursement policy changes and hospital financial challenges.

Health technology assessment (HTA) has developed and evolved in response to the expansion of new medical technologies that have been incorporated into health systems with little evidence to support them. The process health systems use to determine adoption/coverage of new and emerging medical technologies varies greatly among payers, hospitals and other medical providers in the US and among other high-income countries.[1, 13] Because insurers and single payer-national health systems ultimately pay for the majority of medical services, they have been more attuned to incorporate HTA into their policies. Therefore, HTA has become commonplace among many payers, and US public payers are likewise moving towards implementing HTA programs.[1, 13]

2.2 Hospital-Based Health Technology Assessment

The first published article describing a hospital committee evaluating a new technology was in 1986.[14] Since then, HB-HTA programs have gained interest among policy-makers because of its potential for improving new technology adoption decisions.[2] There have been many published articles discussing the value of HB-HTA such as Coye and Kell's [15] article on how hospitals confront new technology (2006), as well as a book entitled, "Hospital-Based Health Technology Assessment" (2016) by Sampietro-Colom and Martin [1] that include descriptions of programs in Canada, Australia, the US and abroad. The authors included twenty-five HB-HTA case studies including US based Kaiser Permanente, Penn Medical Center for

Evidence-Based Practice, programs from northern European countries, as well as other low resource countries such as Brazil.

There are some US HB-HTA programs like the one at University of California San Francisco (UCSF) that began implementing their HB-HTA in 2006 and described how they implemented their model and results in 2011.[16] UCSF described how they emphasized the inclusion of physician leaders in their process. One of their key lessons learned was that instituting an HB-HTA created an evidence-based culture at their institution for new technology adoption. Their program resulted in a reduction of low value new technology adoption requests because the authors concluded that, for many providers, it was not worth going through the process. UCSF's approach offers a model for a hospital considering an HB-HTA program for a US hospital.

Finland has a well-established HTA program for their health system and began implementing an HB-HTA with its 100 province hospitals in 2006.[17] Despite many efforts to implement a successful HB-HTA program, Finland did not have the outcome they anticipated. They implemented a well-funded and comprehensive initiative, approaching each hospital from a collaborative perspective, but the impact of HB-HTA on hospital decision-making remained low. The difficulties identified in the Finnish case study included lack of managerial and physician commitment to HTA in the hospital environment, as well as HB-HTA adoption decisions were inefficient, (a year, on average) resulting in clinicians losing commitment and interest.

Based on these two case studies, key elements for a successful HB-HTA program can be inferred. The main three elements that appear to be critical for success include 1) having strong executive support (e.g., CMOs office), 2) organizational support (e.g., finance, specific hospital departments) and 3) developing a responsive decision process that can efficiently make decisions

(e.g., within three months). UW Medicine had not routinely utilized evidence-based methods for making adoption decisions for new technologies until the implementation of Smart Innovation in 2017, a hospital-based health technology assessment (HB-HTA) program.

2.3 About UW Medicine

UW Medicine is comprised of four large hospitals and other affiliates including Harborview Medical Center, UW Medical Center, Northwest Hospital & Medical Center, Valley Medical Center. In 2018, UW Medicine had 64,220 inpatient admissions, 1.6 million outpatient visits, employed over 30,000 employees and had an annual revenue of $5 billion.[18]

In 2015, UW Medicine's supply chain implemented a value analysis team to improve economic efficiencies in contracting and procurement for UW Medicine. The value analysis team utilizes evidence, data and analytics to improve the pricing, contracts and procurement of new medical supplies. UW Medicine's efforts to affect the cost curve in medical costs have brought tangible savings. However, it didn't address new and emerging medical technologies, therefore Smart Innovation dovetailed well with supply chain efforts.

In 2015, UW Medicine was awarded a four-year grant from The Center for Medicare and Medicaid Innovation (CMMI) totaling $32 million for care transformation that include six main strategies, including Smart Innovation.[19, 20] The proposal was designed to incorporate the Affordable Care Act into UW Medicine's care transformation and help clinicians develop quality improvement strategies. The six strategies included 1) promoting effective, efficient and high value care, 2) better use of data and patient voices to direct care, 3) populations as well as patients, 4) Healthy care as well as sick care, 5) fully developed medical home, and 6) Smart Innovation.

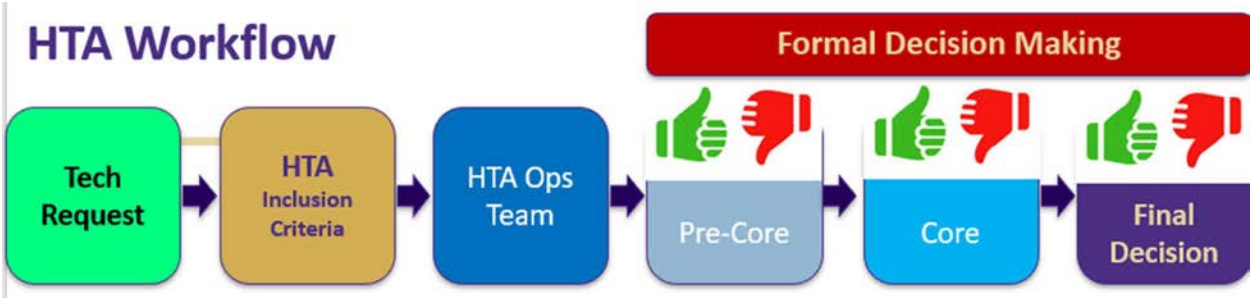
2.4 SMART INNOVATION

Smart Innovation incorporates HTA methods and best practices that have been developed and established from US payers and European health systems as well as other HB-HTA programs. [1, 13, 21] Smart Innovation is a comprehensive HB-HTA program and incorporates executive leadership, finance, and clinicians. The decision framework integrates physician led committees as well as an executive committee that is multi-disciplinary. Smart Innovation's foundational principles are that healthcare technologies are assessed using an evidence-based approach to ensure they add value to patient care and respond to the needs of UW Medicine clinicians and patients. Smart Innovation approaches technology reviews through a broad health care system lens and acts as the single "front door" for new technology requests.

2.5 SMART INNOVATION REVIEW PROCESS

The technology assessment process can begin when a new technology has obtained United States Food and Drug Administration (FDA) or other appropriate regulatory bodies approval and a UW Medicine clinician decides they want to pursue its use. A UW Medicine clinician typically reaches out to procurement department, departmental clinical committees or Smart Innovation to begin the review process (Figure 2.1. Smart Innovation Decision Framework).

Figure 2.1. Smart Innovation Decision Framework



1) **Tech Request** is when a clinician requests the use of a new technology
2) **HTA Inclusion Criteria** is the fiscal threshold the new technology needs to meet before a review begins
3) **HTA Ops Team** is the Smart Innovation work group and staff that leads the program
4) **Pre-Core** is the process Smart Innovation and the clinical sponsor gather evidence and develop the HTA report and presentation to the clinical committee
5) **Core** is the clinical committee that reviews the evidence and makes recommendations to the executive committee for adoption consideration
6) **Final Decision** is the final phase of the decision-making process and is conducted and executed by the executive committee.

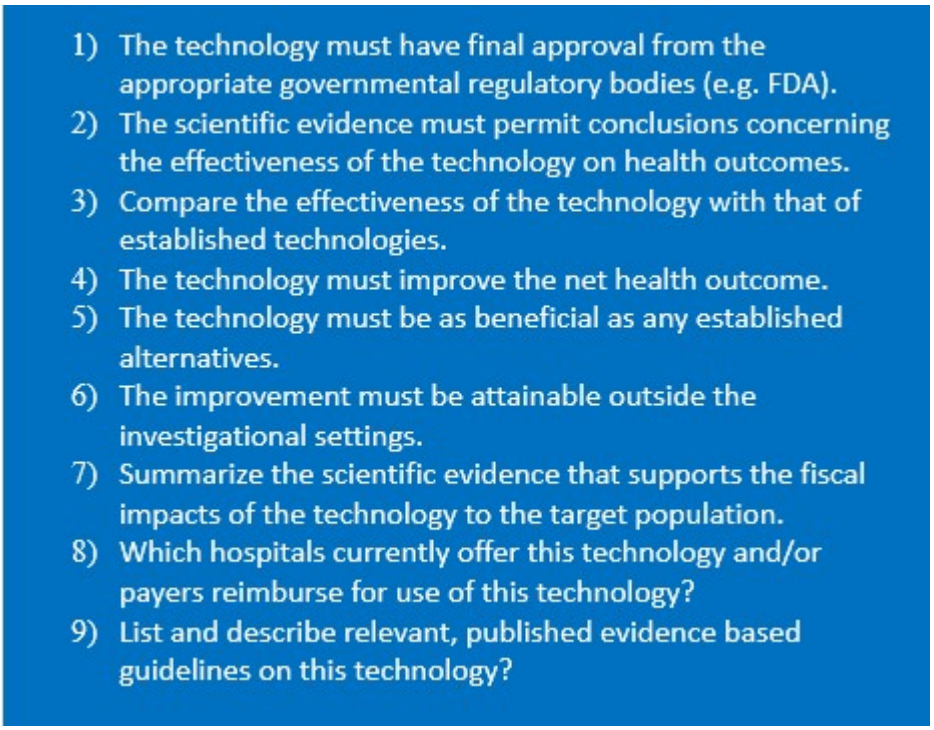
Once the new technology is received by Smart Innovation, it undergoes a first level review that determines if it meets the annualized cost and/or the per procedure threshold. The financial thresholds include technologies for clinical screening, diagnosis and treatment that constitute more than $50,000 annualized cost increase (aggregated across the system), more than $1,000 cost increase per procedure. Smart Innovation can also review a new technology that represents a new clinical treatment paradigm.

Smart Innovation's first course of action when the technology is approved for review is to assess the available evidence by 1) reviewing data from existing HTA reports if available (e.g. The National Institute for Health and Care Excellence (NICE), Emergency Care Research Institute (ECRI) and Agency for Healthcare Research and Quality (AHRQ)), 2) searching the published literature for available studies, 3) reviewing data from payers both public and private to ascertain any coverage policies and or HTA reports (e.g. CMS, Blue Cross Blue Shield), and

4) searching for any publicly available clinical guidelines. The next key piece of data needed for the review is fiscal data, which provides an estimated cost impact of implementing a new technology. Smart Innovation staff coordinate with the finance department to provide details about the new technology (e.g., current procedural terminology (CPT) codes, DRGs).

Smart Innovation staff contact vendors regarding their new technology as well as make an effort to identify the correct contact within their organization that has access and knowledge of the evidence relevant to the review. Smart Innovation also sends the vendor a questionnaire that includes the nine dimensions of evidence [22] (Figure 2.2) and requests that they provide input for the review. This provides the manufacturer the criteria Smart Innovation uses in evaluating their technology and the opportunity for external stakeholder engagement.

Figure 2.2. Nine Dimensions of Evidence



2.6 HTA Report

The next key step in the process is to develop the HTA report. The report structure is based on HTA best practices [13] and includes specific UW Medicine information such as clinical rationale, utilization, current/existing technologies, patient care, and the estimated financial impacts of implementation; as well as payer coverage decisions and national clinical guidelines.

Depending on the type of technology, it may require different types of fiscal or patient quality of care assessment. For new devices or lab tests, the HTA report will include a budget impact analysis and clinical evidence review. For capital purchases, our fiscal office will complete a business plan, net present value (NPV) report, and/or return on investment (ROI) report.

Smart Innovation staff review and synthesize available published scientific studies and exclude vendor marketing materials in the HTA reports. Smart Innovation designates and ranks the quality of evidence based on the GRADE guidelines by Guyatt et al.[23]

Smart Innovation staff meet with clinical sponsors to review the HTA report and ensure it is clinically accurate. Once the HTA report is completed, the clinical sponsor and Smart Innovation staff co-develop a presentation for the appropriate clinical review committee. Smart Innovation staff finalize the HTA report and the chair of the clinical committee sends it out for review in advance of the meeting. Smart Innovation staff and the clinical sponsor present the HTA report to the clinical committee and lead a discussion regarding the published evidence and estimated impact of implementing the proposed new technology.

The HTA report will include a recommendation of adopt, do not adopt, adopt with conditions, or adopt with evidence. The clinical committee will consider the evidence in the HTA report and make a recommendation to UW Medicine's executive committee. The executive committee has broad representation and makes final adoption decisions for UW Medicine. If the clinical committee indicates the technology should not be adopted, that will be the final decision. If the clinical committee recommends to adopt, adopt with conditions, or adopt with evidence, the final decision lies with the executive committee.

For all HTA reports, Smart Innovation staff includes a methodology to monitor and evaluate post adoption impacts on estimated clinical and economic outcomes. Smart Innovation evaluates the implementation of a new technology decision following a year of implementation. Smart Innovation has an appeal process that offers the clinical sponsor a pathway to re-evaluate the technology if new evidence or pricing becomes available after six months of the decision. To date, there has not been an appeal.

2.7 RESULTS

Between July 2017 and April 2019, Smart Innovation has reviewed a total of eleven medical technologies. These have comprised of five laboratory tests, three software assisted systems, two surgical devices, and one capital purchase (Table 2.1). During this period, the total estimated cost savings was over $5 million dollars. We describe three of the eleven HB-HTAs, whereas one was covered and adopted, one was covered with evidence and one was not covered. Smart Innovation's first HB-HTA, completed in July 2017, was a liver ablation technology for treating hepatocellular cancer. The existing technology was radiofrequency ablation (RFA) and the new technology for consideration was microwave ablation (MWA). MWA technology improves patient outcomes by reducing the number of procedures and adverse events such as bleeding. MWA also cost approximately $8,000 less per patient when incorporating disposables and other procedural elements. The liver ablation technology assessment provided clear evidence and was approved by the executive committee.

Table 2.1. Budget Impact of Smart Innovation

Description	Adopt	Estimated Budget Impact
Liver ablation technology for treating Hepatocellular cancer (microwave)	Yes	- $1.2 Million
Urine-based bladder cancer screen	No	- $1.5 Million
DNA test that assesses organ health by measuring allograft (Kidney transplant) injury	Yes-Adopt with evidence	0
Multiple spot laser photocoagulation treating retinal disorders	Yes	- $8,533
Autoimmune encephalitis and paraneoplastic antibody testing for complex neurological disorders	EMR ordering guidance	- $485,000
Computer-Guided Glucose Management System	Pending Finance	NA
Inpatient testing for inherited causes of venous thromboembolism	No	- $50,000
Tablet-based system for managing hospital cardiac arrests (code blue).	No	- $49,000
Video-based monitoring system to observe patients at risk for falls in hospitals.	Yes	- $226,818
Genetic sequencing test for cancer of unknown primary	No	- $2.13 Million
Stent System that can be broken off (external) and used internally.	No	- $226,954
Total Estimated Savings		**-$ 5,876,305**

One of the five laboratory medicine technologies that Smart Innovation reviewed was a urine-based bladder cancer diagnostic and patient monitoring test. The technology was exciting for patients that would prefer to use a simple urine sample for screening as opposed to undergoing an invasive cystoscopy procedure and biopsy. UW Medicine conducts approximately 507 bladder cancer screens per year, and if adopted, it would total over $1.5 million in estimated increased costs annually. Smart Innovation's evidence review indicated that urologists would still need to confirm a high proportion of the urine-based results with cystoscopy because of the

lack of specificity of the test (60% specificity). The average cost of cystoscopy and biopsy at UW Medicine is approximately $875 and the urine-based test is $2,900. The evidence was thus determined to be insufficient to adopt this technology based on both validity and cost-comparison concerns.

A key challenge to implementing Smart Innovation was how to address promising new technologies that lack a body of published evidence. Sorenson, Drummond, and Burns propose how Europe and the US could approve new technologies without clear evidence by introducing a few alternative approaches to address this difficulty.[24] One approach is to "adopt with evidence" which closely monitors promising new technologies via registries. For example, one of the laboratory medicine HB-HTAs was a promising new advance in DNA sequencing to identify allograft injury among patients with kidney transplants. If the test proves to be successful, it has the potential to improve survival among patients with kidney transplants.

For this allograft injury DNA test, the FDA required all labs and medical providers to participate in a CMS registry. This created a strategy for UW Medicine to support promising medical innovations and by monitoring them for safety and efficacy. If there are poor patient outcomes related to the technology it can quickly be identified, and other patterns of care could be documented for review. Patient registries can provide the manufacturer and UW Medicine with the ability to demonstrate a technology's ability to deliver improved health outcomes by having details reported to a centralized monitoring system.[25]

2.8 Next Steps for Smart Innovation

Smart Innovation has evolved from a pilot project to an established initiative at UW Medicine. Smart Innovation will be developing a plan to scale the program and be incorporated

into more clinical departments. This will allow Smart Innovation to identify key clinical partners at UW Medicine and further develop collaborations around new technology assessment and implementation. The program began as a system to review new technologies, but did not emphasize existing technologies or the review of capital purchases. Smart Innovation plans to expand into reviews of capital purchases and existing medical technologies that have indications of poor performance and high cost. UW Medicine leaders are considering incorporating capital purchases and the review of poor performing technologies is being discussed by Smart Innovation and Supply Chain management. UW Medicine is currently implementing a new centralized procurement software that identifies new technologies (medical purchases) that need to be evaluated by Smart Innovation. This will provide Smart Innovation with a method to identify all new technologies that are being requested at UW Medicine and minimize any adoption/procurement of new technologies through alternative back channels.

2.9 Conclusions

Smart Innovation is a collaborative initiative and supports the interests of physicians, administrators, and patients. The program has demonstrated the value of implementing an HB-HTA at UW Medicine and the program will continue to grow and evolve. Smart Innovation has achieved cost savings, avoided uncertain or low-value technologies, and assisted in the implementation of new technologies that have strong evidence. The keys to its success have been the program's collaborative and efficient decision-making systems, partnerships with clinicians, executive support and proactive role with vendors.

Chapter 3. APPLICATION OF HEALTH TECHNOLOGY ASSESSMENT (HTA) TO EVALUATE NEW LABORATORY TESTS IN A HEALTH SYSTEM: A CASE STUDY OF BLADDER CANCER TESTING

3.1 INTRODUCTION

Hospital clinical laboratories are under significant pressure from clinicians and vendors who are promoting the use of new test modalities, more recently often focused on molecular diagnostic techniques. Such new laboratory tests frequently claim to be integral parts of a precision medicine approach, to improve diagnostics, and to be less invasive, more accurate, and offer earlier diagnoses. Such tests are typically send-out tests performed at non-local laboratories which can incur substantial institutional costs for a hospital. A subset of these tests has uncertain sensitivity and specificity and lack data supporting broad use.

With rapid growth in available laboratory tests, clinical laboratories are faced with a challenge of balancing two types of fundamental error: 1) making new laboratory tests available that are inaccurate or, 2) denying access to cutting edge diagnostics that are clinically beneficial or more precise compared to current diagnostic methods.[26] The fiscal risk of adopting new tests can also be significant. Most new tests are initially offered at three times the cost of current practices. The cost of these tests can be fiscally challenging if they are not reimbursed by the Centers for Medicare and Medicaid Services (CMS) or commercial payers (e.g., Regence, Premera Blue-Cross, Kaiser). This can lead to uncompensated costs for the hospital.

With the implementation of a hospital-based health technology assessment (HB-HTA) program, Smart Innovation[27] and development of a Laboratory Formulary Committee, our institution has been able to integrate HTA practices into laboratory medicine, aiming to steward precious healthcare resources by adopting for use only those laboratory tests with strong evidence.

Bladder cancer is diagnosed in more than 70,000 patients in the US every year and in over 430,000 patients globally, making it the 4th most common cancer in men and the 11th most common cancer in women.[28] Localized bladder cancer can be categorized into two main groups: muscle invasive and non-muscle invasive. Those with non-muscle invasive bladder cancer comprise 70% of incident bladder cancer cases. These tumors are characterized by a high rate of recurrence in the bladder necessitating frequent surveillance.[29] UW Medicine conducts approximately 500 bladder cancer screens (cystoscopies) per year. Surveilling recurrent urothelial carcinoma (UC) of the bladder requires frequent cystoscopy, which involves insertion of a cystoscope to the bladder via the urethra, and urine cytopathology. Urine cytopathology has fair interobserver concordance (kappa = 0.32, average chance-corrected agreement including low and high-grade tumors) suggesting the need for a more objective urine-based test.[30] These tests can be expensive and time-consuming for patients; indeed, bladder cancer has higher per-lifetime, per-patient cost than most forms of cancer.[31]

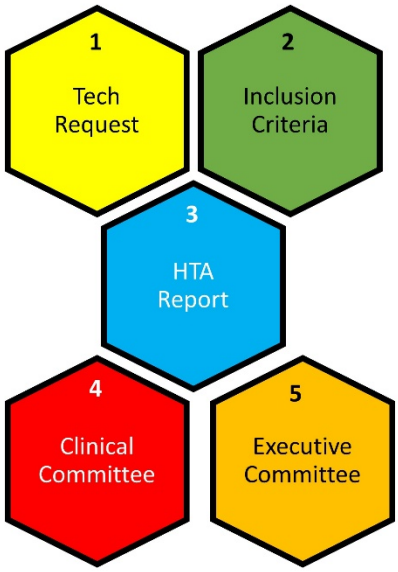
The Laboratory Formulary Committee was approached by a urologist interested in utilizing a newly available send-out molecular bladder cancer test for initial diagnosis and for surveillance of recurrent disease. The proposed test (Cxbladder, Pacific Edge Cancer Diagnostics) is a urine-based molecular test and therefore offers a less invasive screening option for patients compared to the current gold standard, cystoscopy and cytopathology. The

Cxbladder test uses quantitative polymerase chain reaction (qPCR) techniques to analyze messenger ribonucleic acid (mRNA) expression levels of four genes associated with urothelial cancer and one gene involved in inflammatory responses. When utilized for surveillance, the test combines the urine-based gene expression findings with patient clinical data to help determine the probability of the presence of urothelial cancer.[32]

3.2 METHODS

Following the physician request to have the use of Cxbladder reviewed by the Laboratory Formulary Committee, the Laboratory Medicine Department contacted Smart Innovation staff to determine if the new bladder cancer test should go through Smart Innovation's decision framework and evidence review. The Laboratory Formulary Committee is made up of 24 voting members and 5 non-voting members. Among the voting members there were four that were laboratory medicine directors and twenty that were non-laboratory medicine clinicians. The non-voting members include physicians and Smart Innovation staff, and the chair of the committee is the Chair of Laboratory Medicine. It was decided that the test met program inclusion criteria and Smart Innovation began the process to lead the technology assessment of the new test for adoption consideration.[27] Smart Innovation's decision framework consists of five formal steps[27] and included nine dimensions of evidence.[22] The program engages with a clinical committee as well as a hospital executive committee for formal decision-making (Figure 3.1. Smart Innovation Decision Process).

Figure 3.1. Smart Innovation Decision Process



For the review of Cxbladder, Smart Innovation utilized a set of decision-making processes to evaluate the new test and engaged the technology sponsor (the clinical laboratory/urologist) as well as UW Medicine's multi-disciplinary Laboratory Formulary Committee, finance, administration, physicians and physician leadership.[27] The committee approved its use on a limited basis by a single urologist for cases meeting a narrow definition: negative cystoscopy and atypical/suspicious urine cytology. Following a decision by the Committee a case series review was performed for twelve patients: six who had received the test in the subsequent year following the adoption decision, and six patients evaluated for suspicion of recurrent bladder cancer prior to the adoption decision. A Pathologist at our institution summarized the physician notes and patient charts by categorizing the outcome variables; and described the observed differences in clinician decision-making and patient outcomes. Outcome variables included the type and number of follow-up tests conducted, their results, and results of

subsequent cystoscopy, cytopathology, imaging studies, biopsy procedures, and, if applicable, repeat Cxbladder testing. Test turn-around-time (TAT) in days was assessed from time of sample collection to time of resulting into medical record.

In December 2019, Smart Innovation collaborated with Laboratory Medicine to conduct a post-decision analysis on the Cxbladder pilot study. We selected twelve patients of a single urologist at our institution. The twelve patients each had a negative cystoscopy and an atypical or suspicious urine cytology result. Group One included six patients tested with Cxbladder between January 2018 and December 2019 (Table 3.2). For all six patients, a negative cystoscopy result and atypical or suspicious cells on one or two successive urine cytopathology tests prompted the physician's decision to send the Cxbladder test. Search functions of our institution's pathology database were utilized to identify a similar group of patients (Group Two), comprised of patients seen by the same urologist who were found to have atypical or suspicious urine cytopathology but between 2016 and 2017 when Cxbladder was not available. The search was then narrowed to those noted to have negative cystoscopy at the time of urine collection, similar to the group tested with Cxbladder, yielding six patients for Group Two in the case series (Table 3.3).

Table 3.2. Clinical Data from Cases with Cxbladder Testing (Group One)

Age	Tumor Type	Cytopathology	Cxbladder™ Test	TAT * (days)	Result	Management	Outcome
76	non-invasive, high-grade	suspicious cells	MONITOR	9	Score: 7.4; Clinician-directed Protocol	biopsy	POSITIVE for recurrence
69	non-invasive, low-grade	atypical cells	DETECT	9	Score: 0.04; Normal Gene Expression Score, 97% NPV	surveillance cystoscopy/cytology q 6 months + BCG	no recurrence identified x 1.5 years
66	invasive, low-grade	highly atypical cells x 2	MONITOR	13	Score: 4.3; Clinician-directed Protocol	surveillance cystoscopy/cytology q 6 months	no recurrence identified x 1 year
60	invasive, high-grade	rare atypical cells x 2	MONITOR	10	Score: 3.0; Low Probability, 97% NPV	cystoscopy in one year	cystoscopy at one year negative
83	invasive, high-grade	atypical cells	DETECT	6	Score: 0.07; Normal Gene Expression Score, 97% NPV	surveillance cystoscopy/cytology q 3 months + BCG	no recurrence identified x 1.5 years
69	invasive, high-grade	suspicious cells	DETECT	6	Score: 0.18; Elevated Gene Expression Score	surveillance cystoscopy/cytology q 6 months + BCG	6 month cytology POSITIVE for carcinoma
		suspicious cells	DETECT	7	0.72; High Gene Expression Score	biopsy	POSITIVE for recurrence

*TAT: turn around time

Table 3.3. Clinical Data from Cases without Cxbladder Testing (Group Two)

Age	Tumor Type	Cytopathology	Cxbladder Test	TAT* (days)	Result	Management	Outcome
74	non-invasive, high grade	highly atypical cells				biopsy	POSITIVE for recurrence
56	non-invasive, high grade	rare atypical cells				surveillance cystoscopy/cytology q 3 months + BCG	suspicious cystoscopy at 1 year, biopsy = NEGATIVE, no recurrence identified x 4 years (death by other causes)
76	non-invasive, high grade	suspicious cells				surveillance cystoscopy/cytology q 3 months + mitomycin C	suspicious cystoscopy at 1 year, biopsy = POSITIVE for recurrence
83	non-invasive, low grade	rare atypical cells				surveillance cystoscopy/cytology q 3 months + valrubicin	positive cystoscopy at 2.5 years, biopsy = POSITIVE for recurrence
56	invasive, focal high grade	rare atypical cells				surveillance cystoscopy/cytology q 3 months + BCG	no recurrence identified x 4 years
82	invasive, high-grade	rare atypical cells				surveillance cystoscopy/cytology q 3 months + mitomycin C	no recurrence identified x 3 years (death by other causes)

*TAT: turn around time

We also evaluated whether Cxbladder testing was associated with a difference in the number of tests ordered (cytologies, cystoscopies, biopsy) between Groups One and Two. Patients were followed for at least twelve months following an atypical urine cytology and the counts of tests between the two groups were compared using the non-parametric analysis of variance (ANOVA) Kruskal-Wallis test.

3.3 Results of the Health Technology Assessment

Published evidence

The published clinical data available for Cxbladder contained mixed evidence. One vendor-funded published study demonstrated a sensitivity of 90% and specificity of 60% for Cxbladder compared to the gold standard (cystoscopy and biopsy).[33] The study compared urine-based testing to cystoscopy, and used a total of 1,036 urine samples collected from 803 patients undergoing surveillance for urothelial cancer. An Agency for Healthcare Research and Quality (AHRQ) funded systematic review that evaluated urinary biomarkers for diagnosis of bladder cancer, including Cxbladder, found a high rate of false positives and that accuracy is poor for low-stage and low-grade tumors.[34] The systematic review also presented one study that was published in 2012 and funded by the vendor in which the accuracy of Cxbladder indicated medium-risk of bias with a reported sensitivity of 0.82 (CI, 0.70 to 0.90) and specificity of 0.85 (CI, 0.81 to 0.88) for evaluation of symptoms, for a positive likelihood ratio (LR) of 5.53 (CI, 4.28 to 7.15) and a negative LR of 0.21 (CI, 0.13 to 0.36).

Conclusions from the AHRQ's systematic review included: "Urinary biomarkers miss a substantial proportion of patients with bladder cancer and are subject to false-positive results in others." They also specified there's not enough current medical evidence to show that using

tumor marker tests compared to standard tests to look for bladder cancer leads to more health benefits and that more medical studies are needed. Results from AHRQ's analysis of Cxbladder included the following: 1) demonstrated that strength of evidence = as low, 2) reporting bias = not detected, 3) precision = indicated imprecise, and 4) consistency = could not be determined.

Clinical Guidelines for Bladder Cancer Screening

At the time of the review, there were no national clinical guidelines that recommended using Cxbladder for bladder cancer screening. The American Urological Association (AUA) published guidelines on the evaluation of microscopic hematuria in adults. They recommended cystoscopy for adults over age 40, as well as for adults younger than 40 if they had risk factors for developing bladder cancer.[35] The National Institute for Health and Care Excellence (NICE) 2015 bladder cancer diagnosis and management guidelines did not indicate using urine-based testing (including Cxbladder) for diagnosing and monitoring bladder cancer. They recommend using cystoscopy as the gold standard.[36] The National Comprehensive Cancer Network (NCCN) does not address Cxbladder specifically, but recommended consideration of urine biomarker tests for monitoring disease recurrence.[37] Major national health insurers were assessed for coverage options and Premera-Blue Cross, a primary carrier in our region indicated a non-coverage policy for Cxbladder, considering it experimental.[38] At the time of the assessment, there was not a US National Coverage Decision (NCD), and the Center for Medicare and Medicaid (CMS) did not cover Cxbladder.

Other HTA reports

During our review in 2017, we searched for other HTA reports and found one conducted by Emergency Care Research Institute (ECRI). There were no HTA reports by the Washington State Healthcare Authority Health Technology Assessment Program. The ECRI report reviewed Cxbladder for the indication of monitoring patients with a confirmed bladder cancer diagnosis. Two key conclusions from the ECRI HTA report included: 1) "Cxbladder use does not completely obviate the need for routine cystoscopy" and 2) "additional studies of Cxbladder that focus on extended follow-up are required." ECRI recommended that future studies should quantify the proportion of patients receiving false-negative results and be appropriately compared to cystoscopy to achieve a better balance between patient quality of life (decreasing invasive cystoscopy) and ensuring cancer recurrence is identified prior to any serious health concerns.[39]

UW Medicine, Fiscal Impact Analysis

The fiscal impact of adopting Cxbladder at our institution, in addition to, but not replacing, the current cystoscopy with and without biopsy exams, was estimated at $1.5 million dollars annually. When assessing our average cost to screen and monitor for bladder cancer: $900 per cystoscopy (with and without biopsy) and total cost per year $450,000 to the additional cost of Cxbladder: $3,000 per test and total cost per year $1.5 million, Cxbladder was estimated to be more than three times the cost of cystoscopy and urine cytology (approximately 500 tests per year). Suggestive or positive Cxbladder tests would need to be followed up with cystoscopy, so it was determined that "replacement" of cystoscopy would not entirely occur, therefore not offering economic or clinical efficiency; and the true cost would include current testing methods

(cystoscopy, biopsy, cytology, imaging) as well as Cxbladder. There are other costs associated with Cxbladder testing that were not detailed in our fiscal report that add to the overall cost. These include unnecessary office visits, and other laboratory testing costs.

Adoption Decision

The Laboratory Formulary Committee reviewed the available evidence with the requesting clinician and determined that given the low specificity of the test, the fiscal impact, and lack of coverage by primary health insurers in the United States, the hospital would be incurring the cost of the test without likely reimbursement at low yield for patients. Therefore, Smart Innovation and the Laboratory Formulary Chair recommended that additional published data was necessary before the test would be approved for use for bladder cancer monitoring or surveillance.

After reviewing the evidence, members of the Laboratory Formulary Committee voted to not adopt Cxbladder system wide; however, to support a pilot study for the requesting urologist for the stated indication: “an equivocal visualized lesion with atypical urine cytology” which was estimated to be approximately 10 patients per year. This recommendation was unanimously approved by the clinical committee, was reviewed and approved by our executive committee, and the policy went into effect January 2018.

3.4 Pilot Study

Patients in both groups were in a similar age range (Group One: range 60-83 years, median 69 years;-Group Two: range 56-83 years, median 75 years). All twelve patients had a history of papillary urothelial carcinoma, high-grade or low-grade, invasive or non-invasive, in

both groups as indicated in Tables 3.2 and 3.3. All patients had received prior rounds of Bacillus Calmette Guerin (BCG) therapy with or without resection.

The Cxbladder test was sent nine times for the total of six patients in Group One. One test was rejected due to kit expiration and one test was rejected due to sample stability. One patient was tested twice. The provider/clinic variably ordered the Cxbladder MONITOR test or the Cxbladder DETECT test, due to availability of kits placed in clinic by the manufacturer, despite the tests' indications for suspected recurrence, which would suggest use of the MONITOR test. The seven Cxbladder test results varied for each pilot case with values ranging from 0.04 to 7.4, and results of normal (n=2), low probability (n=1), elevated gene expression score (n=1), high gene expression (n=1), and clinician directed protocol (n=2). Both patients with a normal score received surveillance cystoscopy and cytopathology (one every three months, one every six months) with BCG and did not receive a biopsy.

In Group One, recurrence was identified by the time of conclusion of this study in two of the six patients (median follow-up of patients without recurrence was 22 months at conclusion of this study (range 16 months to 27 months). One of the patients with a low probability score was followed with cystoscopy in one year, which was negative. The two patients with "clinician-directed protocol" scores were treated differently based on clinician judgement: the first with a history of high grade bladder cancer and the higher score (7.4 with range of clinician directed protocol from 3.5-10.0) underwent a biopsy which was positive for recurrence; the second patient, with a history of low grade non-invasive bladder cancer and a lower score (4.3), underwent surveillance cystoscopy/cytopathology at six-month intervals, with no recurrence identified by the time of conclusion of this study. The patient tested twice initially received an elevated gene expression score which gave a "low probability of urothelial cell carcinoma", and

was followed with surveillance cystoscopy and cytopathology at six-month intervals with BCG; however, the six-month cytopathology was positive for carcinoma. At that time a second Cxbladder was sent, which demonstrated a high gene expression score. A biopsy demonstrated recurrence of the patient's carcinoma. For the two patients in Group One found to have recurrent carcinoma within the study time-frame, time to detection of recurrence was 64 days and 308 days. In total, the patients in Group One received 10 urine cytologies, 9 cystoscopies, and 1 biopsy in the first year following each patient's initial atypical cytology result.

In Group Two, the group not receiving Cxbladder, five of six patients were managed with surveillance cystoscopy and urine cytopathology every three months with variable therapies including BCG, mitomycin C and valrubicin. For one patient with highly atypical cells on cytopathology, a biopsy was performed one month after the initial cytology result and was positive for recurrence. For the remaining five patients, if at any point cystoscopy returned positive, biopsy was performed. In total, three of the six patients in Group Two were found to have recurrent carcinoma within the study time-frame, with time to detection of recurrence of 37 days, 343 days and 1,014 days. Median follow-up of patients without recurrence was 35 months at conclusion of this study (range 31 months to 52 months). In total, the six patients in Group Two received 14 urine cytologies, 13 cystoscopies and 3 biopsies in the first year following each patient's initial atypical cytology result.

The counts of follow-up tests for both groups are displayed in Table 3.4. There was not a statistically significant between-group difference in follow-up tests ordered (p-value = 0.15).

Table 3.4. The Number of tests ordered based on Group in one year*

Group	# of Cytologies	# of Cystoscopies	# of Biopsies
Group One	10	9	1
Group Two	14	13	3

*Data limited, in both groups, to the first twelve months following atypical cytology.

3.5 DISCUSSION

Making HTA decisions can be difficult when a new technology has yet to develop a large body of evidence including real world data. This leaves decision makers with a level of uncertainty that can only be addressed prospectively: 1) by waiting for new published evidence (by other institutions) or 2) by conducting pilot studies. Therefore, HTA committees tend to lean more on the conservative side of adoption decisions to abate the risk of poor patient outcomes and unnecessary costs from adopting new and uncertain technologies.

The HTA decision process for Cxbladder was able to weigh the financial risk and the potential added improvement for managing certain bladder cancer patients. This is where difficulty can arise in a clinical committee, and challenges the competing interests of clinicians who seek new advantages when managing complex patients and HTA experts who are concerned with the fiscal impacts and are without the needed evidence to make a clear recommendation. In our clinical committee, the discussion addressed these issues and eventually landed on not adopting system-wide, but to pilot Cxbladder.

What we learned from this new approach was if we would have made a safe and low risk decision to not adopt and not pilot, we would have missed an opportunity to identify a certain patient profile that can benefit from Cxbladder testing. Patients with normal cystoscopy and

atypical cytology, use of Cxbladder led to fewer follow-up cystoscopies, cytologies and biopsies with the same proportion of patient's with recurrence detected within one year (two of six in each group). We also learned that following up on HTA decisions is important and collaborating with our clinicians derives a true partnership as well as improved insights for clinical guideline development. Smart Innovation will continue to consider this type of HTA decision pathway (do not adopt – pilot), and our leaders and staff now have the confidence and understanding about how to better balance competing interests among clinicians, fiscal impacts and HTA.

There is research interest in better understanding the real-world data related to using Cxbladder for bladder cancer screening and monitoring. A recently published study (Koya et al, 2020)[40] used 443 Cxbladder MONITOR tests among 309 patients at three hospitals in New Zealand. The authors indicated that Cxbladder MONITOR was able to identify 77.8% who were safely managed with one cystoscopy per year. The authors concluded, "Including Cxbladder MONITOR in the protocol for patient surveillance provided clinical utility by reducing the average number of annual cystoscopies by approximately 39%." The non-vendor funded study may offer insights for urologists who are monitoring patients with known UC, however, the generalizability may not be representative to all US hospitals because of the difference between single and pluralistic payer systems, and Cxbladder is not widely reimbursed in the US.

The HTA evaluation of Cxbladder demonstrated that adding an alternative HTA decision pathway (do not adopt – pilot) provided the ability to pilot a new molecular test that in traditional HTA programs would not have been implemented. The pilot study offered our HTA body, the Laboratory Formulary Committee and clinicians at our institution the benefit of collecting real world data following our HTA decision. Cxbladder performed better than cytology and other

non-invasive tests, as well as trended to a reduced number of cytologies, cystoscopies, and biopsies among certain patients, although the difference did not reach statistical significance.

The case series demonstrated relatively consistent surveillance management of patients with atypical or suspicious cytology prior to the limited use of Cxbladder. After piloting Cxbladder for this subset of patients, high scores on Cxbladder, with suspicious cytopathology, appeared to move the provider to perform a biopsy sooner than in the provider's standard of care practice; two patients had intermediate score recommending "clinician directed protocol" and the management differed in each based on the provider judgement, one undergoing biopsy with cancer recurrence detected and the other monitored with surveillance and no recurrence was identified within the follow-up period. Some patients with negative and low scores of Cxbladder received less-frequent follow-up surveillance than had been the provider's usual care based on evaluation of management in Group Two.

3.6 CONCLUSIONS

We found the HTA process was more efficient and less resource intensive than conducting a broad-based study with a large sample size; and provided policy decisions that reflects the published evidence, clinical guidelines as well as actual clinical practice. Our HTA decision regarding Cxbladder will continue to be monitored to ensure patients are afforded accurate and early diagnosis of bladder cancer by ongoing review of emerging research, as well as clinical guidelines. The results of the pilot study indicated that among a narrow patient profile selected, Cxbladder assisted the pilot urologist in ordering confirmatory testing and a reduction in number of follow-up cystoscopies, cytologies, and biopsies within one year.

Chapter 4. ASSESSING THE EARLY IMPACT OF A HOSPITAL-BASED HEALTH TECHNOLOGY ASSESSMENT (HB-HTA) PROGRAM, SMART INNOVATION.

4.1 INTRODUCTION

The use of formal health technology assessment (HTA) is now considered common practice by national health systems and insurance companies to inform new technology adoption and reimbursement decisions. HTA is less common within hospitals and health systems.[1] The premise of hospital-based health technology assessment (HB-HTA) is that more informed and structured decisions about the adoption and use of health technologies will improve clinical outcomes and hospital efficiency.[27, 41] The emergence of HB-HTA activities are derived from the necessity to mitigate the risk of adopting new technologies without sufficient evidence of clinical benefit and potential cost impact.[1] Given that most hospitals make technology decisions at the system level, clinical efficacy, safety, utilization and cost data should be used to inform these decisions.[27, 41] However, new technology decision-making in hospitals is influenced competing interests among various stakeholder groups, including clinicians, hospital financial leadership, patients, and contracted vendors.[27] As hospitals in the United States (US) have different cultures and processes in place, and additionally differ in several respects with counterparts in other countries, there is no one-size fits all HB-HTA model, and varying approaches to implementing programs within a hospital are common.[1]

In 2017, the University of Washington Medical Center (UWMC), a Seattle-based integrated hospital system with four hospital campus and affiliates, designed, developed and implemented an HB-HTA program called Smart Innovation. We describe Smart Innovation in

more detail in a previously published paper.[27, 41] In brief, the program provides a process and decision framework to evaluate new technologies objectively, and it works with clinical and executive committees to inform adoption decisions.[27, 41] Smart Innovation brings together stakeholders from hospital administration, clinical leadership, finance, purchasing, and supply chain to optimize new medical technology adoption decisions.[27, 41] There are very few HB-HTA programs in the US and a paucity of data evaluating these programs.[2] This paper reports on the impact of two early technology assessments undertaken through Smart Innovation.

We compared UWMC's adoption and diffusion of two medical devices and their associated surgical procedures to matched control hospitals in the US. We selected one technology that did not undergo formal HB-HTA assessment and was adopted without restriction, the Sentinel™ filter cerebral protection system for transcatheter aortic valve replacement (TAVR) as a control. We then selected a device that underwent a formal HB-HTA review, microwave ablation (MWA) for treating hepatocellular carcinoma. These technology adoption decisions were conducted during the early phase of Smart Innovation, with MWA serving as the institution's first HB-HTA review.

4.2 Medical Technologies

Transcatheter aortic valve replacement (TAVR) procedures with the Sentinel™ cerebral protection system

The Sentinel™ filter for TAVR procedures was approved by the US Food and Drug Administration (FDA) in 2019.[42] The purpose of the Sentinel™ filter is to prevent aortic wall debris and blood clots from reaching the brain and causing stroke in patients who undergo a TAVR procedure. It is a single-use device and the filters are designed for immediate removal

once the TAVR procedure is complete.[43] At the time of FDA approval, there was limited evidence available to formally assess efficacy, safety and budget impact to the hospital. The UWMC thus adopted the Sentinel filter + TAVR procedure without a formal HB-HTA review. We selected this technology as a control given that it did not undergo formal HB-HTA.

Liver Ablation for Treating Hepatocellular Carcinoma

Radiofrequency ablation (RFA) and microwave ablation (MWA) are therapeutic modalities for treating hepatocellular carcinoma. RFA technology was initially approved by the FDA in 1995 for treating cardiac disorders and was later used off-label for liver tumor ablation.[44] The MWA device that we evaluated was approved by the FDA in 2017.[45] The therapeutic effect of both methods relies on thermal injury, but MWA uses an electromagnetic field as opposed to the electrical current used in RFA.[46] Data support the contention that MWA can reduce hospital readmission rates for additional ablation treatments, since MWA can target larger tumors when compared to RFA. However, large-scale, randomized, prospective clinical trials are needed to understand more completely the clinical and patient outcome difference between RFA and MWA.[47]

Clinicians at UWMC requested permission to use MWA technology, and the Smart Innovation program was therefore asked to conduct a technology assessment and make recommendations to the clinical and executive committees regarding adoption. Smart Innovation conducted an HTA including evidence synthesis, budget impact analysis, clinical guideline review, a survey of insurance coverage, and a review of MWA's safety, efficacy and comparative performance versus RFA technology. MWA was approved for adoption in July 2017 and implemented at UWMC in January 2018, and we selected MWA for this study because seven quarters of post-adoption data were available for this analysis. The MWA adoption was

implemented at the same hospital (UWMC) as the TAVR Sentinel™ filter, which also made it a good comparator.

4.3 Hypotheses

We hypothesized that the adoption rate for TAVR procedures with a Sentinel™ cerebral protection system would not differ between UWMC and control hospitals over a similar time period. Conversely, we hypothesized that there would be a difference in adoption of MWA at UWMC as compared with control hospitals that was temporally related to the HB-HTA intervention. Furthermore, we hypothesized that a different MWA adoption rate at UWMC versus control hospitals would be associated with cost savings.

4.4 Methods

We conducted a retrospective, observational study from October 2015 to December 2019. The study population included UWMC and seventeen control hospitals, and we selected controls using specific inclusion and exclusion criteria as well as medical procedure codes to gather utilization data to compare control hospitals to UWMC. We compared UWMC to controls between pre-intervention and post-intervention periods, which were separated by the point in time where UWMC implemented TAVR and MWA. There are two main dimensions in these analyses: Hospitals and Procedures.

Hospital Control Selection Process: Inclusion and Exclusion Criteria:

We identified candidate control hospitals based on inclusion criteria gathered from Vizient's database, supplemented with data from the American Hospital Association (AHA) to establish a list of potential controls (Tables 4.5, 4.6) based on hospital characteristics and surgical volume. Vizient is a national group purchasing organization that serves 95% of academic medical centers in the US.[48] The AHA maintains the largest database of hospitals in the US and is a national organization that represents all hospitals.[49]

We established unique inclusion criteria for control hospitals by procedure based on UWMC's bed capacity, the number of TAVR and MWA procedures conducted at UWMC, and whether the control was an academic medical center. To identify a sample of potential controls for each procedure, Vizient database was queried to find hospitals with a similar range of hospital beds and procedures to UWMC, with the goal of finding a minimum of five control hospitals for each procedure that had similar characteristics to UWMC.

For TAVR procedures, the control hospitals' inclusion criteria included: 1) the number of hospital beds must be between 400 and 800, 2) the control hospitals needed a total of more than 400 TAVR procedures in 2018 & 2019, and 3) must be an academic medical center. For exclusion criteria, control hospitals for TAVR procedures must not have evidence of using the Sentinel™ filter device based on that device's unique billing code. These criteria provided twelve control hospitals for TAVR.

For MWA procedures, the inclusion criteria included: 1) number beds between 300 and 900, 2) more than 100 total liver ablation procedures in 2018 & 2019, and 3) must be an academic medical center. These criteria yielded eleven control hospitals. Because RFA and MWA share the same billing codes, Vizient's data could not be used to differentiate between the

two technologies, so we contacted each of the eleven potential MWA control hospitals to determine which met exclusion criteria. The exclusion criteria for the MWA control hospitals included the following: 1) hospitals with a formal HB-HTA program and 2) hospitals using the same technology as UWMC (MWA). We removed those meeting exclusion criteria, which left five control hospitals the for MWA analysis.

Table 4.5. TAVR Procedures for UWMC and Control Hospitals

Hospital	**Ownership Type***	**Number of Beds***	**Number of Annual Admissions***		**Number of Annual Surgical Procedures***		**Number of Annual TAVR Procedures**		**% of Procedures that were TAVR**	
			2016	**2018**	**2016**	**2018**	**2016**	**2018**	**2016**	**2018**
UWMC	Non-Government/ Non-Profit	492	18362	19350	15895	16475	282	331	1.77%	2.01%
Controls	Non-Government/ Non-Profit =11; Non-Profit/ Church Operation = 1	Range 459 - 793	Range 19880 - 41472	Range 20379 - 41113	Range 10146 - 34681	Range 10843 - 37778	Range 87 - 278	Range 133 - 414	0.56%	0.67%
		Mean 612	Mean 30925	Mean 31685	Mean 34403	Mean 36405	Mean 192	Mean 243		

* Provided by the American Hospital Association (AHA)

Table 4.6. MWA Procedures for UWMC and Control Hospitals

Hospital	**Ownership Type***	**Number of Beds***	**Number of Annual Admissions***		**Number of Annual Surgical Procedures***		**Number of Annual MWA Procedures**		**% of Procedures that were MWA**	
			2016	**2018**	**2016**	**2018**	**2016**	**2018**	**2016**	**2018**
UWMC	Non-Government/ Non-Profit	450	18362	19350	15895	16475	131	108	1%	0.66%
Controls	Government / State Owned = 4; Non-Government/ Non-Profit =1	Range 306 - 888	Range 13780 - 33117	Range 14967 - 35074	Range 10273 - 53463	Range 11018 - 50189	Range 33 - 108	Range 46 - 150	0.24%	0.31%
		Mean 606.4	Mean 28126	Mean 28455	Mean 28403	Mean 28643	Mean 67.8	Mean 90.2		

* Provided by the American Hospital Association (AHA)

4.5 Analysis: TAVR and MWA Procedures

We utilized surgical procedure billing codes to gather TAVR and MWA surgical data. The level of analysis for both technologies was at the hospital level and patient and hospital data were aggregated into quarters. The main outcome variable of interest was the number of procedures per quarter, and the data was acquired from a US national claims database (Vizient), and was gathered for seventeen quarters between October 1, 2015 – December 30, 2019.

We conducted descriptive analyses to evaluate UWMC's and control hospitals' utilization by comparing mean utilization before and after the intervention, and we visualized the trends by plotting the number of TAVR and MWA procedures over time. To aggregate utilization trends for TAVR and MWA procedures, we calculated arithmetic and weighted means for number of procedures per quarter. Weights were based on the total number of surgical procedures for UWMC and each control hospital in the pre- and post-periods. We then compared the arithmetic and weighted means to determine if they were different by assessing the percent differences between the pre- and post-periods. We concluded that there was no difference in results based on using either arithmetic or weighted means, and thus we used the arithmetic means to aggregate control hospitals in these analyses.

We evaluated the individual hospital characteristics and surgical volume in both UWMC and control hospitals for each technology and surgical procedure, in order to ensure the controls were well-matched. We summarized the number of procedures per quarter for each hospital, and compared the percent difference between pre- and post-period trends in utilization for UWMC and controls. For TAVR and MWA procedures, we evaluated whether UWMC matched well to control hospitals and if we observed a difference among utilization trends between UWMC and controls.

In addition to descriptive data analyses to measure the effect of Smart Innovation, we employed a difference-in-differences (DID) analytic approach. We first evaluated whether utilization trends were equivalent across UWMC and controls in the pre-period (parallel assumption) by plotting utilization curves for UWMC and controls. Because visual assessment can be subjective, we then conducted a multivariable regression model for the number of procedures per quarter for TAVR and MWA in the pre-period to test for statistical significance for the interaction between group status (UWMC vs. control) and time (quarter), while adjusting for several hospital characteristics in the pre-period. Hospital characteristics assessed for adjustment included the number of acute care beds, as well as hospital-level patient demographics from TAVR and MWA procedures (age, gender, race, payer type, comorbidities).

For TAVR and MWA procedures, we performed regressions using ordinary least squares (OLS) in the DID models to adjust for hospital level heterogeneity using demographics that were gathered for each of the seventeen quarters in this study. Analyses were performed using the R statistical software [(R (v4.0.2, [50] using RStudio v1.3.1073)] yielding p-value significance of differences between UWMC and controls for the number of procedures per quarter. Human subjects review was approved by the University of Washington Medical Center's Institutional Review Board (IRB).

The DID analysis used outcome-specific multivariable regression models, adjusting for hospital characteristics for TAVR and MWA. For each DID model, the main outcome measure included the number of procedures per quarter, and the primary covariate of interest (DID estimator) was the interaction between time and intervention, where time was pre- and post-HB-HTA decision (0= pre, 1=post) and intervention was the implementation of HB-HTA policy decisions at UWMC (0=controls,1=UWMC). The p-value was used as the measure for statistical

significance. The DID models were therefore used to test whether Smart Innovation policy decisions impacted utilization at UWMC. Adjustments to the model were made for age, gender, race and payer type, comorbidities, and the number of acute care beds for TAVR procedures, while adjustments for age, gender, race, payer type, and the number of acute care beds were used for MWA procedures.

4.6 RESULTS

The control hospitals for TAVR and MWA procedures matched well to UWMC based on teaching status, number of hospital beds, number of admissions and the number of TAVR and MWA procedures (Tables 4.5, 4.6), although among controls for the TAVR procedure, all twelve were non-profits whereas UWMC is a state-owned entity. Because the controls had not adopted the Sentinel™ filter, they may have had a common approach to reviewing/adopting new and high-cost devices, but this cannot be stated with certainty. Conversely, as regards the control hospitals used for the MWA procedure analysis, ownership/state-owned status was similar. For both TAVR and MWA procedure control hospitals, the proportion of these selected procedures to total surgical procedures was higher at UWMC than at control hospitals.

TAVR Procedures

Comparisons of average patient age, percent male, percent white, percent Medicare enrollee, percent with comorbidities, and the number of acute care beds between UWMC and controls in the pre- and post-periods for TAVR procedures are shown in Table 4.7. There was a significant difference between average age, percent Medicare, and the number of acute care beds between UWMC and controls, and all covariates were adjusted in the regression.

Table 4.7. TAVR Hospital Level Characteristics, UWMC and Control Hospitals, October 2015-December 2019

Variable	UWMC	Control Hospitals	Standardized Mean Difference
age (mean (SD))	77.09 (1.64)	79.99 (2.26)	1.472
male (mean (SD))	59.31 (5.64)	53.69 (7.94)	0.817
white (mean (SD))	90.68 (5.31)	86.47 (12.37)	0.442
Medicare (mean (SD))	83.69 (4.27)	90.23 (7.12)	1.113
comorbid (mean (SD))	89.58 (3.44)	89.11 (5.95)	0.097
acute care beds (mean (SD))	396.00 (0.00)	582.58 (109.81)	2.403

*standardized mean difference over 1

We observed a 10% reduction in the number of TAVR procedures between the pre- and post-periods when comparing percent change between UWMC to controls (Table 4.8). There were eight control hospitals with a higher percent change (pre-post periods) when compared to UWMC, and four that had a lower percent change compared to UWMC. Based on our trend plot, we did not observe a difference in utilization trends between UWMC and controls during the time of this study (Figure 4.1).

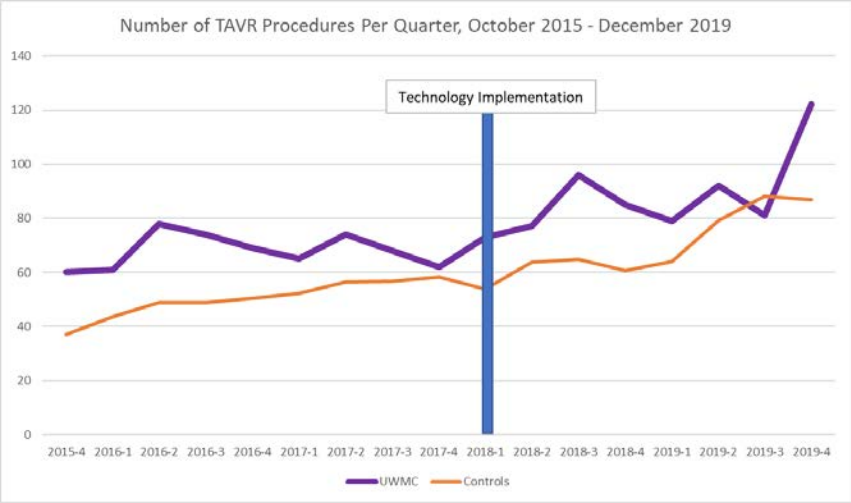
In addition to descriptive data analyses to estimate the effect of Smart Innovation, a multivariate DID analysis was used to test the difference between UWMC and controls for the number of procedures per quarter in the pre-and post-periods. Potential confounding variables were selected a priori for the regression: age, race (percent white), gender (percent male), payer type (percent Medicare), comorbidities (Elixhauser co-morbidity index score of 1 or more); and the number of acute care beds. After adjusting for covariates, the DID estimator was -1.5, indicating no statistically significant change in utilization between pre-and post-Sentinel Filter + TAVR implementation (p-value: 0.87). The DID estimator indicates the change in the number of

TAVR procedures per quarter between pre-and-post periods, which was 1.5 less per quarter for UWMC when compared to controls. The number of acute care beds and comorbidities were significantly different between UWMC and controls (p-value of < 0.05).

Table 4.8. Mean TAVR Procedures Per Quarter, Pre and Post Periods

Hospital	Pre	Post	Percent Change
UWMC	68	88	30%
Controls	50	70	40%

Figure 4.1. The Number of TAVR Procedures Per Quarter



MWA *Procedures*

For MWA procedures, we compared patient average age, percent male, percent white, percent Medicare, and the number of acute care beds between UWMC and control hospitals between October 2015 and December 2019 (Table 4.9). The number of acute care beds differed significantly between UWMC and controls, and this was adjusted for in the DID regression

models. When comparing the number of MWA procedures at UWMC to controls, we observed a strong difference in utilization between pre- and post-periods at UWMC versus control hospitals. There was an increase in the number of MWA procedures per quarter between the pre- and post-periods at control hospitals, yet at UWMC MWA decreased (Table 4.10). UWMC also experienced a downward trend in the number of procedures over the study period, whereas control hospitals experienced an upward trend during the same time period (Figure 4.2).

Table 4.9. MWA Hospital Level Characteristics, UWMC and Control Hospitals, October 2015-December 2019

Variable	UWMC	Control Hospitals	Standardized Mean Difference
age (mean (SD))	62.65 (1.50)	62.01 (3.05)	0.263
male (mean (SD))	65.71 (11.07)	61.09 (16.83)	0.324
white (mean (SD))	73.59 (9.98)	79.93 (11.14)	0.599
Medicare (mean (SD))	46.76 (10.44)	43.51 (12.16)	0.287
acute care beds (mean (SD))	396.00 (0.00)	580.25 (194.04)	1.343

*standardized mean difference over 1

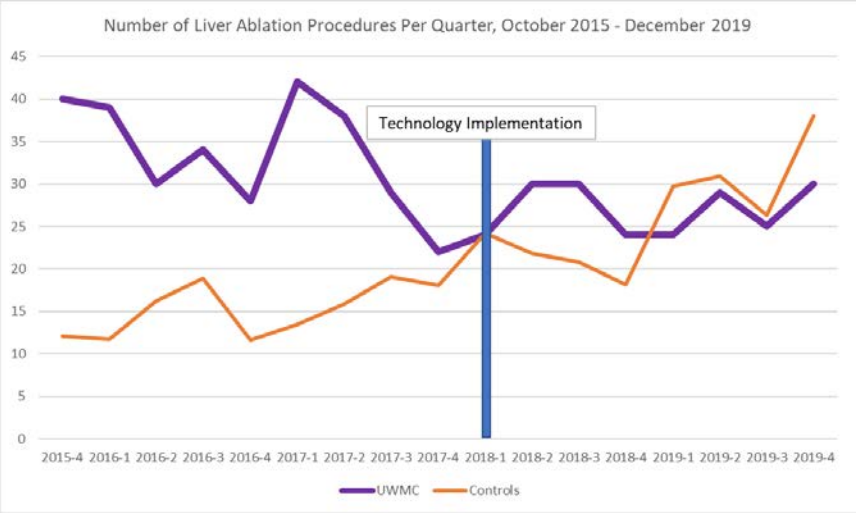
UWMC's percent change between the pre- and post-period for the number of MWA procedures per quarter was the most reduced compared to individual control hospitals and the difference in percent change was 51% (Table 4.10). In addition to descriptive data analyses to estimate the effect of Smart Innovation, a multivariate DID analysis was used to test the difference between UWMC and controls for the number of procedures per quarter in the pre-and post-periods. Potential confounding variables were selected a priori for the regression: hospital level age (average age), race (percent white), gender (percent male), payer type (percent Medicare); and the number of acute care beds. After adjusting for covariates, the DID estimator was -18.8, indicating a statistically significant change between pre-and post-intervention time

periods in utilization, relative to the MWA HB-HTA policy decision (p-value: 0.0007). Only age was found to be a significant covariate between UW and control hospitals in this analysis (p-value of < 0.05). The DID estimator indicates the change in the number MWA procedures per quarter between the pre-and post-periods, which was 18.8 less per quarter for UWMC when compared to controls.

Table 4.10. Mean MWA Procedures Per Quarter, Pre and Post Periods

Hospital	Pre	Post	Percent Change
UWMC	33.56	27.00	-20%
Controls	19.92	26.06	31%

Figure 4.2. The Number of MWA Procedures Per Quarter



We observed a difference in total costs when comparing UWMC to controls between the pre and post periods (Table 4.11). Total costs for liver ablation procedures rose modestly at control hospitals but decreased at UWMC. Specifically, UWMC spent $1,702,444 more than

control hospitals prior to the HB-HTA intervention, whereas it spent $647,658 dollars less than controls after the intervention. The difference in total costs is consistent with the MWA utilization trends seen in Figure 4.2, the percent change between UWMC and controls in Table 4.10, and the DID results for MWA.

Table 4.11. Total Cost for Liver Ablation Procedures, UWMC and Controls, October 2015 – December 2019

Hospital	Total Cost Pre	Total Cost Post
UWMC	$ 3,597,607	$ 1,852,974
Controls	$ 1,895,163	$ 2,500,632
Difference	$ 1,702,444	$ (647,658)

4.7 DISCUSSION

This study assessed the early impacts of implementing the Smart Innovation program at UWMC. We presented the results from a new technology that did not undergo Smart Innovation review and was adopted without restrictions (TAVR). We then evaluated a surgical device adoption decision that underwent review through the Smart Innovation decision framework. We thereby gained insights about surgical trends associated with adopting new technologies in the hospital setting with and without the use of HB-HTA methods.

Based on our analyses, there was a slight difference between UWMC and controls for the technology (TAVR) that did not undergo HB-HTA review that did not achieve statistical significance. The technology that was reviewed by Smart Innovation at UWMC, however, appears to have decreased significantly, with financial savings.

The overall increasing trend in the number of TAVR procedures for both UWMC and controls during the time of this study (Figure 4.1) likely reflects what is occurring in hospital

practice, as TAVR procedures are increasing based on demand and hospitals have responded by increasing the number of procedures over time.[51] Adoption of the TAVR Sentinel™ filter without Smart Innovation review is therefore a reasonable target for evaluation and comparison to the effect of HB-HTA because it reflects a real-world example of a medical device that occurred organically without high-level scrutiny or intervention. The independent DID test results for each of the two technologies allowed this study to determine whether our HB-HTA approach, Smart Innovation, makes an impact on the real-world data for adopting new medical technologies.[52]

A key assumption using DID models is the parallel trend assumption, i.e. the assumption that outcome data will maintain parallel trends in the prior to intervention.[53] Because visual inspection of parallel trends can be subjective, we conducted a multivariable DID regression to empirically test if there was a significant difference in pre-period. These DID models indicated that the difference between UWMC and controls were not statistically significantly for the number of TAVR and MWA procedures in the pre-period.

4.8 LIMITATIONS

We acknowledge potential selection bias related to control hospital and technology selection. We selected control hospitals with very narrow inclusion and exclusion criteria. For example, if a potential control hospital had a HB-HTA program or had made similar technology decision as UWMC, they were excluded in this study. There was a small sample size for the hospital controls (n=17) and technology comparisons were limited to two. We selected MWA and TAVR technologies because they were implemented in the pilot phase of Smart Innovation's development and provided a longer time of study for this analysis (post-period). Among some

controls, the counts of procedures per quarter were small for comparing utilization between UWMC and controls. Furthermore, the analysis may not be generalizable to US hospitals that are not academic medical centers, have hospital bed size and surgical volume outside of control inclusion criteria and have different utilization trends among the technologies being reviewed in this study.

We did not identify the number of surgeons that conducted MWA or TAVR procedures among the hospitals in this study. Hospitals could have recruited or lost TAVR or MWA surgeons during the time of this study, which could have had an impact on the number of procedures. Hospitals could have also increased or decreased their marketing efforts for these procedures and may have impacted the number TAVR and MWA procedures. Therefore, the number of procedures conducted at UWMC and controls may be explained by the change in personnel and varying marketing efforts by an individual hospital.

One of the DID model challenges was identifying potential confounding variables either observed or unobserved prior to the study, and we were limited to variables available in Vizient's database. However, DID designs assume that confounders varying across the groups are time invariant, and time-varying confounders are group invariant.[52] One of the potential unknown factors that we did not account for is the time it takes for control hospitals to make adoption decisions and incorporate new technologies into care. The actual uptake of the new technologies was not available as our count data only indicated the number of procedures performed, and not which type of technology was used (e.g., old versus new technology).

Because comorbidities were captured using diagnostic related group (DRG) data, which are used for inpatient procedures only, we were not able to capture comorbidities for procedures that were conducted in an outpatient setting. TAVR procedures were conducted in the inpatient

setting, liver ablation procedures were conducted in a mix of inpatient and outpatient. Therefore, we were not able to adjust for comorbidities in the MWA DID models.

4.9 CONCLUSIONS

This study reviewed two medical technologies at the hospital level and evaluated utilization based on adoption decisions that were made with and without the support of Smart Innovation at UWMC. HB-HTA has the potential to improve hospital outcomes, however, is not common in the US. This analysis provided insights from a quantitative evaluation of a new HB-HTA program and how UWMC compared to other similar hospitals regarding new technology adoption and diffusion. When UWMC used HB-HTA methods for technology adoption there was a difference in utilization when compared to controls; and when UWMC adopted a new technology without using HB-HTA methods there was no difference in utilization. When UWMC used HB-HTA methods, there was a reduction in total costs when compared to controls following HB-HTA policy decisions. The difference in utilization observed to be correlated to HB-HTA was associated with a large decrease in total cost.

Chapter 5. CONCLUSION

This dissertation research describes UW Medicine's experience implementing a formal HB-HTA program called Smart Innovation. These studies were designed to inform hospital policy by improving UW Medicine's approach to new technology adoption. Smart Innovation was initially a pilot and began as a grant funded program. Following implementation and promising early results, it was incorporated into UW Medicine's Supply Chain Management. The early results demonstrated that HB-HTA can be implemented successfully, achieve

significant cost avoidance and savings, and offer alternative HB-HTA policies to pilot uncertain new technologies.

We designed and implementation Smart Innovation based on strengths and weaknesses that were published as “lessons learned” by other programs. We ensured the program had strong executive support from the Chief Medical Officer (CMO), the assistant CMO, Chief Finance Officer, and other key hospital leaders. It was critical to have executive support because HB-HTA programs disrupt existing decision-making processes and institute a new framework for reviewing and adopting new medical technologies. As expected, during our rollout, we experienced pushback from clinicians and hospital departments at UW Medicine that wanted to retain decision-making authority, and without executive support it would have been very difficult to successfully implement Smart Innovation.

Another important strategy for promoting Smart Innovation’s success was to turn around new technology decisions as rapidly as possible. This helped in establishing rapport with clinicians who were interested in adopting new technologies quickly. However, it was logistically challenging to develop rigorous evidence for the HTA reports in a short time. One of the biggest challenges in developing HTA reports was the fiscal analysis. We did not have the time, nor the staff, to complete empiric budget impact analyses (BIA) or cost-effectiveness analyses (CEA). We also initially had difficulty obtaining utilization and cost data from UW Medicine Finance because of bandwidth problems in that division. Although Smart Innovation’s data requests did not receive priority initially, over time, we were able to rely on a dedicated staff for Smart Innovation data requests.

Despite the inherent challenges that Smart Innovation faced, the program was implemented successfully, and it demonstrated its value to hospital leadership, department heads,

and clinician leaders. This dissertation research faced related challenges, as I was tasked with implementing a new and logistically complex program while simultaneously evaluating it.

This dissertation included a case study on one HB-HTA, Cxbladder, which is a new molecular test for bladder cancer. We described in detail how we evaluated Cxbladder including the published evidence, the HTA report, our experience discussing new test at clinical and executive committees, as well as the policy decision. In the process of the Cxbladder HB-HTA, Smart Innovation developed a novel approach to HB-HTA decisions, namely not to cover a technology system-wide, but to pilot it. The pilot was to test Cxbladder among a small number of patients meeting specific clinical criteria and to assess its diagnostic yield. The decision to use a pilot program stemmed from a request by a urologist who sought to use the test for only one specific clinical context, and permission for the pilot was granted, for approximately ten patients over a year, because the Cxbladder HB-HTA did not have sufficient evidence to render an informed decision. The pilot study thereby provided an opportunity to partner with the pilot urologist and the Department of Laboratory Medicine. Overall, the Cxbladder HB-HTA process yielded beneficial results. UW Medicine saved approximately $1.5 million annually by not adopting Cxbladder system-wide, and we also learned how it performed in the clinical context studied in the pilot.

Even though the sample size of the Cxbladder pilot was small, the real-world data from generated lead to a revised decision for use of Cxbladder at UW Medicine. The change allowed all urologists at UW Medicine to use Cxbladder in monitoring patients who have had urothelial carcinomas but present with atypical urine cytology and negative cystoscopy biopsies. The pilot results indicated that those receiving Cxbladder testing had a reduction in other diagnostic screening when compared to similar patients who did not receive Cxbladder screening. Thus, our

evidence, which is limited, nonetheless indicates that Cxbladder in this specific use case may offer an alternative assessment that can reduce other diagnostics for certain patients. Whether or not this approach is cost-effective or beneficial to morbidity or mortality will require a larger study that incorporates more patients than this limited pilot study.

The last study in this dissertation research estimated the early impact of implementing Smart Innovation at one of the four UW Medicine hospitals, University of Washington Medical Center (UWMC). Even though this was an ambitious and challenging objective, we were able to develop an analytic approach that compared UWMC's surgical utilization and overall costs with seventeen similar academic medical centers using insurance claims data. We selected two new surgical devices that were considered for adoption at UWMC, one that was reviewed by Smart Innovation and one that was not. The technology that was not reviewed by Smart Innovation did not appear to be utilized differently over time or in comparison to peer institutions, but when UWMC utilized HB-HTA for a second technology, utilization of that second technology, was reduced when compared to other similar academic medical centers, and this reduction was correlated with a reduction in total costs. This finding is of significance because there are very few HB-HTA programs in the US, and even less that have been quantitatively evaluated, so this counts as among only a few demonstrations of the value of this approach. We believe that the analytical model we employed can be replicated by other HB-HTA programs, and that other sites can gain insight and into the quantitative impacts of HB-HTA programs in their own settings.

Smart Innovation began as a voluntary pilot where hospital departments and clinicians had the option to utilize the program. I am grateful for those hospital departments and individual clinicians who participated in Smart Innovation early on, and thereby allowed me to review the new medical technologies they were interested in adopting. Without those volunteers, Smart

Innovation would never have been successful, and this research would never have occurred. One of the most active and collaborative departments was the Department of Laboratory Medicine, and I truly appreciate their engagement with the program.

After the program was formalized at UW Medicine, Smart Innovation began to experience increases in new technology review requests. The program began to strengthen and build momentum. Smart Innovation was operating regular meetings to consider new technology requests as well as expand into new areas of UW Medicine. Unfortunately, after a change in system leadership, the program did not receive the same level of executive support. Also, during this critical time of transition, COVID-19 became the hospital's number one priority. The COVID-19 crisis caused serious programmatic challenges overall, but specific challenges resulted from UW Medicine's stoppage of elective surgeries and diversion of clinical staff to other areas. Along with many hospital initiatives, Smart Innovation was no longer able to operate in the same manner.

Nonetheless, despite the challenges that this dissertation research faced, including COVID-19, changes in leadership, and hospital financial uncertainty, Smart Innovation was successfully implemented and this dissertation research was completed. We learned from our experience implementing Smart Innovation that HB-HTA is a powerful tool that hospitals can implement to control costs and improve the quality of technology that it allowed to be used within the health system. HB-HTA programs can achieve substantial cost savings and cost avoidance, they can guide and evaluate pilot programs for new technologies, and they can improve decision-making processes in hospitals by grounding them in evidence-based reasoning.

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VITA

Erik Landaas has over twenty-five years of healthcare leadership experience including public health, epidemiology, policy, health technology assessment, health insurance and payer delivery systems, as well as health outcomes and quality assurance. Erik has consulted with medical start-ups by developing evidence and economic strategies to develop market access. Erik graduated with his Masters in Public Health from the University of Washington and has a passion for improving healthcare systems that benefit patient outcomes.