



# The Intersection of Medicine and Business: Applying Business Principles and Strategy to Better Understand Surgical Costs, Innovation, and Payment Reforms

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Citation	Leya, Gregory. 2018. The Intersection of Medicine and Business: Applying Business Principles and Strategy to Better Understand Surgical Costs, Innovation, and Payment Reforms. Doctoral dissertation, Harvard Medical School.
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# **Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School**

**Date:** 28 March 2018

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**Scholarly Report Title:** The Intersection of Medicine and Business: Applying Business Principles and Strategy to Better Understand Surgical Costs, Innovation, and Payment Reforms

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## **ACKNOWLEDGMENTS**

I first and foremost want to thank Dr. Tsuyoshi Kaneko for sponsoring this Scholarly Project. Dr. Kaneko has served as my primary clinical and research mentor for the past two years, and he has played an instrumental role in guiding my career trajectory and research skills. In addition to Dr. Kaneko, Dr. Louis Nguyen and Dr. Thomas Feeley have been invaluable mentors to me and have developed my dual interests in business and surgery. Finally, I am extremely grateful to Dr. Christiana Beveridge, Dr. Sofia Warner, and Dr. Sameer Hirji for being my teammates and supportive colleagues through all these projects.

## ABSTRACT

**Purpose:** As an MD/MBA student, I had the opportunity to explore multiple areas of research at the intersection of medicine and business. Increasingly, patient outcomes and quality care are shaped by factors outside of the purview of what physicians learn in medical school and residency. Outcomes and care quality are driven by systems and business considerations, from cost measurement and payment reform to process improvement, technological innovation, and business strategy. My Scholarly Report is a compilation of three research projects that I pursued in collaborations between Harvard Medical School and Harvard Business School and that have since been submitted for publication. Through this work, I hope to better demonstrate how business principles intersect with clinical ideas to shape the future of surgery.

Projects included in this Scholarly Report:

- 1) Journal Article: *Prospective Cost Analysis and Implications of Wound Complications in Lower Extremity Vascular Surgery Procedures*

Purpose: To conduct cost-effectiveness analysis of a new surgical wound dressing to complement a completed clinical trial.

- 2) Book Chapter: *Percutaneous Interventions for Cardiac Valvular Disease: A Review of Contemporary Practices and Future Directions*

Purpose: To summarize the current state of transcatheter therapies in cardiac surgery, both from a clinical and from a business perspective.

- 3) Journal Article: *Hospital-based Accountable Care Organization Success May Be Limited by Ability to Track Performance Indicators*

Purpose: To better understand why Accountable Care Organizations, a cornerstone of the Affordable Care Act, have failed to significantly curb quality and cost shortfalls among U.S. hospitals

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## **INTRODUCTION: COST, TECHNOLOGY, AND PAYMENT REFORM IN HEALTHCARE**

Since the 2001 publication of the Institute of Medicine's report entitled "Crossing the Quality Chasm: A New Health System for the 21st Century," the United States' healthcare system has drawn increased scrutiny for its exorbitant costs and questionable quality. (1, 2) A growing business literature in healthcare highlights that good patient care depends not only on the clinical expertise of the healthcare provider, but on systems and business models that translate clinical knowledge into tangible patient outcomes. (3, 4) Central to these discussions is the realization that, with limited national resources devoted to healthcare, clinicians should not only consider clinical outcomes of new technologies and therapies when making treatment decisions, but they should be cognizant of how using certain treatments depletes resources available to treat other patients. Clinical effectiveness should not be the only criteria used to drive treatment decisions; rather, value, defined as clinical outcomes per unit of cost, is a better driver of treatment decisions in order to create scalable and sustainable solutions to the U.S.'s healthcare woes.

One of the most prominent voices advocating for value in healthcare is Professor Michael Porter at Harvard Business School. As he writes in the *New England Journal of Medicine*: (5)

In health care, value is defined as the patient health outcomes achieved per dollar spent. Value should be the preeminent goal in the health care system, because it is what ultimately matters for customers (patients) and unites the interests of all system actors. If value improves, patients, payers, providers, and suppliers can all benefit while the economic sustainability of the health care system improves. Value encompasses many of the other goals already embraced in health care, such as quality, safety, patient centeredness, and cost containment, and integrates them. It is also fundamental to achieving other important goals such as improving equity and expanding access at reasonable cost.

As the notion of "value" increases in importance in U.S. healthcare discussions, however, clinicians, politicians, and administrators are realizing that the drivers of the U.S.'s colossal healthcare costs are unknown, let alone the most effective methods to curb these growing costs. (6) (7) (8) (9)

This scholarly project, a combination of three separate research projects, seeks to shed light on some of these issues. First and foremost, in order to improve the U.S. healthcare system and propose sustainable solutions, we must first be able to measure quality and costs, the two sides of the value equation. One metric to capture these measurements is cost-effectiveness. The

first research project included in this report demonstrates the methodology of cost effectiveness, and sheds light on the costs associated with poor quality outcomes in healthcare. The second project focuses on new technology development in cardiac surgery. Prof. Michael Chernew and many other economists have attributed a significant share of healthcare expenses in the U.S. to new technology development. (10) Therefore, the clinical and cost-effectiveness benefits of new technologies merit scrutiny, as is done in the included book chapter. Finally, as our ability to measure healthcare costs and quality, and to appreciate the drivers of increasing costs, has grown, national attention has turned to efforts to effectively curb cost growth and improve quality in health care. The final project included in this report closely evaluates Accountable Care Organizations, which are a new provider model that seeks to achieve those goals, and scrutinizes their ability to sustainably improve the value equation in U.S. healthcare.

## **COST-EFFECTIVENESS**

The first research project included in this report is a cost-effectiveness analysis of a silver-eluting wound dressing (Acticoat) that is intended to reduce rates of post-operative infections and wound complications. While the Acticoat wound dressing is more expensive than typical sterile gauze, the increased expense could be justified if the dressing sufficiently reduced hospital lengths of stay and post-operative costs, thus improving patient outcomes. The goal of the manuscript is to reinforce the shifting paradigm that clinical outcomes alone should not be the primary motivator for the adoption of new technologies. Rather, technology adoption should be driven by considerations of how new technologies fit into the overall context of a resource-limited healthcare system. Technology should only be adopted if it provides sufficient value in improving clinical outcomes per unit costs, which can be achieved by either significantly improving outcomes or significantly reducing costs while maintaining current outcomes.

Unfortunately, the clinical trial that paralleled the cost-effectiveness analysis demonstrated no clinical benefit of the Acticoat silver-eluting dressing when compared to conventional sterile gauze. Therefore, by definition, the Acticoat dressing could not be a more cost-effective solution to gauze for wound dressings since Acticoat is more expensive than gauze. Nonetheless, we used cost data from Brigham and Women's Hospital to calculate the costs associated with managing post-operative wound complications. This calculation reveals an opportunity for innovation—by showing the costs associated with wound complications, any

innovation, where a new technology or process innovation, that could reduce the costs or frequency of those complication could provide value in the healthcare system. Wound complications are both bad for patient outcomes and pose a humongous cost burden on our healthcare system.

## **TECHNOLOGY INNOVATION IN CARDIAC SURGERY**

While new technologies are an often-cited contributor to rising healthcare costs, they also significantly improve patient outcomes and have the opportunity to even reduce healthcare costs, depending on the competitive environment for a given technology. One particularly remarkable example of rapid technological development has been the adoption of transcatheter valve therapies in cardiac surgery. Initially introduced in the mid 2000s for pulmonary valve replacements, transcatheter therapies have spread as a treatment modality for all four heart valves and are beginning to supplant conventional open valve replacements as the standard of care. (11)

This trend in cardiac surgery is a classic example of disruptive innovation. Introduced by Prof. Clayton Christensen in 1995, disruptive innovation describes the process by which a new technology establishes itself in simple applications at the bottom of a market and then progressively moves up the market to larger-scale, more complicated applications, eventually displacing established competitors. (12, 13) The bottom of the market is generally used to describe inferior products and traditionally unattractive opportunities for large established incumbent firms. While every industry experiences disruptive innovation in some form, the field of cardiac surgery has been a prime example of disruptive innovation for many decades. Since their introduction in the 1970s and 1980s, stents have grown from being viewed as a significantly inferior solution for high-risk patients to being a reasonable alternative to open coronary artery bypass surgery for many patients. (14) Similarly, just as stents have eaten away at the market size of coronary artery bypass surgery, so too have transcatheter aortic valve replacements, initially viewed as a solution only for high-risk patients who were not surgical candidates, slowly supplanted the open aortic valve replacement market.

In examples of disruptive innovation, incumbent market leaders are often reluctant to adopt potentially disruptive technologies because these new technologies initially represent an inferior technology with limited market value appeal. This trend has also been seen in cardiac surgery with transcatheter aortic valve replacements (TAVR). Many cardiac surgeons were



skeptical of the value of TAVR, allowing interventional cardiologists to take ownership of the procedure. However, now that TAVR is supplanting the traditional open aortic valve replacement market, cardiac surgeons are trying to develop transcatheter procedural skills so that they do not lose too much market share to interventional cardiologists.

The included book chapter highlights the innovative trends in transcatheter therapies, and includes a discussion of disruptive innovation and cost-effectiveness in cardiac surgery. The chapter also highlights an important nuance into how to consider “value” in technology adoption—whereas transcatheter therapies initially were only for high-risk patients and were more expensive than open surgical procedure, providing limited value for the healthcare system, with time there has been increased innovation that has both improved outcomes and reduced costs for transcatheter therapies. Thus, a treatment that initially seemed to provide minimal benefit to the healthcare value equation has become an important contributor to value over the course of a decade. Thus, new disruptive technologies should not be dismissed early on if their value proposition is yet unclear. This observation highlights the importance of a conducive policy environment that allows for disruptive innovation and better patient care, which is the topic of the third project included in this Scholarly Project Report.

## **PAYMENT REFORM AND ACCOUNTABLE CARE ORGANIZATIONS**

With the passage of the Affordable Care Act in 2010, there has been increased attention given to business model and systems solutions that could re-align priorities of hospitals and clinics to reduce cost growth and improve quality. (15-17) Clinically intelligent providers with access to good technology is not sufficient for high-value patient care—rather, infrastructure and incentives must be in place to properly align clinical knowledge and technology to produce high-value solutions. Among the most promising initial proposals to achieve such results were Accountable Care Organizations (ACOs). (18) ACOs are groups of health care providers working together to provide coordinated care for their patients, with the goal of improving quality while avoiding unnecessary services. They are meant to achieve these results through novel payment models (capitated payments) and better monitoring of quality outcomes, corresponding to the two components of the Porter value equation. (19) While ACOs were anticipated to significantly curb cost growth and improve quality, they have had mixed success in achieving these goals. (20, 21)

While the underwhelming achievements of ACOs have been well-described and published, there have been significantly fewer studies explaining why ACOs have fallen short of their goals. The third project included in this Scholarly Project seeks to address exactly that point. Using a nationwide survey of ACOs, we found that ACOs do not even have the necessary infrastructure to track the cost and quality metrics that are necessary to function effectively as an ACO. Instead, we propose bundled payments as an alternative payment model that holds more promise to re-align healthcare providers to provide higher value care.

Together, the above-described projects highlight the important intersection of business and medicine, and demonstrate how both are crucial to providing sustainable solutions to the United States' healthcare woes.

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## STUDENT ROLE

### *1) Cost-effectiveness of silver-eluting, anti-bacterial dressing:*

The idea for this project came from Dr. Louis Nguyen. I assisted in data collection and worked with our statistician in conducting statistical analysis using SAS. I subsequently analyzed our data with assistance from Dr. Louis Nguyen and our statistician, and I wrote the entire manuscript.

### *2) Book chapter discussing trends in the disruptive technological innovation of transcatheter valve replacements*

Dr. Sameer Hirji was invited to write a book chapter on transcatheter therapies in cardiac surgery. I conducted the entirety of the literature search and wrote the entire book chapter. Dr. Sameer Hirji and Dr. Tsuyoshi Kaneko subsequently edited the manuscript prior to submission.

### *3) Analysis of healthcare organizations' preparedness to adopt Accountable Care Organizations*

Dr. Sofia Warner and Dr. Christiana Beveridge had the initial idea to conduct a survey of ACOs across the U.S. They brought me in on the project, and together we narrowed down our research question and the scope of the project. Rather than creating our own survey, we discovered the AHA database and used this survey to conduct our analyses. I worked closely with Christiana to conduct ACO cost and quality analyses, while Sofia Warner focused on bundled payment prospects. The three of us evenly contributed to writing the manuscript.

## **PROJECT 1: COST-EFFECTIVENESS ANALYSIS**

### **Prospective Cost Analysis and Implications of Wound Complications in Lower Extremity Vascular Surgery Procedures**

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Presented at the New England Society for Vascular Surgery and Eastern Vascular Society Joint Annual Meeting 2014, Boston, MA

This work was funded by an unrestricted grant from Smith & Nephew (CKO) and the Lea du Pont Vascular Fund

## ABSTRACT

**Objective:** We sought to quantify the incremental cost of wound complications (WC) in patients undergoing open lower extremity arterial procedures.

**Summary Background Data:** Wound complications (WC) after surgery (surgical site infections [SSI], wound dehiscence, hematoma, seroma), cause significant morbidity and require additional resources to treat. Economic data analyzing the cost burden of post-operative WC are limited.

**Methods:** Hospital administrative accounting cost data from a single tertiary institution was analyzed in patients enrolled in a prospective, randomized trial testing two post-operative wound dressings (gauze vs. silver-coated alginate). Bivariate analyses and multivariable generalized linear models were used to assess the incremental cost of WC at 30 days.

**Results:** Of the 224 patients who underwent lower extremity vascular surgery procedures, 61 (27.2%) developed WC, 40 (17.9%) of which were SSI. Patients with WC had longer mean index LOS (8.2 vs. 6.0 days,  $P=.0025$ ), higher rate of 30-day readmissions (23% vs. 6%,  $P=.0001$ ), and greater mean cumulative 30-day LOS (10.1 vs. 6.2 days,  $P=.0001$ ). The tested dressings showed no efficacy or cost differences. Mean incremental cost of WC was \$11,973 by bivariate analysis, reflecting a 35% higher cost than non-WC patients ( $P=.0112$ ), and \$9,915 by multivariable modeling ( $P=.0037$ ).

**Conclusions:** WC remain a frequent sequela of open lower extremity vascular surgery, with significant cost and resource utilization. Although the tested silver-coated alginate dressing did not demonstrate efficacy in reducing WC, potential cost savings can be captured by new and effective products or by patient care quality improvements.

## INTRODUCTION

Wound complications (WC) cause significant morbidity following revascularization procedures and manifest as dehiscence, seroma, lymphocele, hematoma, and surgical site infections (SSI). Especially burdensome are SSI, which persist as one of the most common post-operative complications and type of nosocomial infection in the United States.<sup>1,2</sup> SSI occur in 4 27% of vascular procedures and not only contribute to patient morbidity and mortality, but result in a substantial economic burden.<sup>3-9</sup> Numerous single institution and database studies have demonstrated both prolonged length of stay and increased total hospital costs associated with SSI,<sup>11-16</sup> though detailed economic data are lacking.

Factors shown to predispose patients to SSI can have both procedure- and patient-specific elements, including incision location, end-stage renal disease, female sex, obesity, and chronic obstructive pulmonary disease, among others.<sup>4,6,10,12,14,17-19</sup> Wounds following lower limb revascularization are particularly prone to infection and dehiscence, with some studies citing rates as high as 44%.<sup>3</sup> Among strategies to prevent SSI are antibiotic and antimicrobial dressings. One such dressing is Acticoat Absorbent (Smith & Nephew PLC, London, United Kingdom), an antimicrobial dressing coated with nanocrystalline silver that delivers up to a 3-day dose of silver ions. Despite the promise of such antimicrobial dressings, no evidence-based recommendations have been issued favoring these dressings over sterile gauze.<sup>20</sup>

Our study herein provides a cost analysis to complement our previously published primary randomized controlled clinical trial, which investigated whether silver-eluting Acticoat dressing was more effective than conventional gauze dressing in preventing lower extremity WC.<sup>19</sup> While the primary study found a 30% incidence of 30-day post-operative WC in our cohort, there was no statistically significant difference in WC rates between the two dressing types. Those results demonstrated that the incidence of WC continues to be unacceptably high and that there is significant room for innovation to reduce the health and economic burden of surgical WC.

The current detailed fiscal analysis sought to quantify the incremental cost of WC in patients undergoing lower extremity vascular procedures. In doing so, we aimed to delineate not only whether certain procedural or patient factors are more strongly associated with increased costs of WC, but to precisely define the total financial burden of WC and the potential cost-savings of new dressing designs or quality improvement strategies.



## METHODS

This study is a cost analysis of a subset of patients from the primary prospective trial that compared silver-eluting alginate (Acticoat) with sterile gauze by following 500 patients undergoing lower extremity arterial vascular procedures at two academic tertiary care medical centers and one Department of Veterans Affairs medical center.<sup>19</sup> Detailed inclusion criteria can be found in the primary trial publication, but to summarize, patients were eligible for participation from October 2010 to September 2013 and inclusion criteria included adults (>18 years old) undergoing non-emergent open surgical procedures below the inguinal ligament for peripheral vascular disease involving arteries or bypass grafts, including common femoral access for EVAR. Exclusion criteria included patients <18 years old, patients with known silver or alginate allergies, participation in another interventional clinical trial, or prior participation in the present study.

The primary study was a prospective, randomized, double-blind design in which the patients were randomized in the operating room, after wound closure but prior to dressing application, to receive either silver-eluting alginate dressing or conventional gauze as the initial wound dressing. Chlorhexidine and general sterile technique, glucose control, and temperature control were also applied as WC prevention strategies per provider and site preferences, but were not recorded. Peri-operative antibiotics were not mandated by protocol, but it is the general practice of most surgeons at our institution to use gram-positive coverage, such as vancomycin and cefazolin. The initial dressing was kept in place until it became grossly soiled, there was a clinical need to remove the dressing, or post-operative day 3, whichever came first. The primary endpoint was the development of a WC within 30 days of the procedure. We used NSQIP WC definitions, which included superficial surgical site infections, deep surgical site infections, dehiscence (requiring local wound care), or other complications (seroma, lymphcele, hematoma, etc.). Data were collected using the Research Electronic Data Capture (REDCap) system and were analyzed as intention-to-treat.

The cost-analysis study presented here uses detailed hospital accounting data for a cohort of 224 patients from one of the two academic tertiary care medical centers in the primary prospective trial. The data includes 30-day hospital-specific costs (as opposed to charges), including both direct costs and indirect costs. Direct costs were defined as procedural costs for the primary, as well as any secondary, procedures, including operating room costs and devices. Indirect costs were defined as hospital costs not accrued during the primary or secondary procedures, including hospitalization and nursing care costs. Further subcategories of cost data were not available. Provider costs were not included in this study. Post-procedural hospitalization duration and re-admissions decisions were left to the discretion of the providing clinician.

We used SAS 9.3 (SAS Institute, Cary, NC) to carry out Wilcoxon rank sum tests for bivariate analysis and generalized linear models (GLM) for multivariable cost models to assess the incremental total cost of WC at 30 days. An initial cost comparison of the silver-eluting alginate and gauze groups was conducted based on the primary study, which randomized dressing type. Subsequent bivariate analyses were conducted using demographic and clinical variables. Variables with a bivariate significance  $P > .05$  were kept in for multivariable analysis, and use of silver-eluting alginate dressing was included as a forced-in variable. This work represents a cost analysis of the primary clinical trial for which approval was obtained from the Institutional Review Boards of the participating sites and informed consent was obtained from participating subjects.

## RESULTS

The primary trial demonstrated an overall WC rate of 30% among the three tertiary institutions, with no significant difference in WC rates between patients who initially received silver-eluting alginate vs. gauze dressing (Odds ratio [OR], 1.03;  $P=.87$ ). In multivariable analysis, significant patient characteristics associated with WC included BMI (OR, 1.05;  $P=.01$ ), absence of a conduit (OR, 0.12;  $P<.001$ ), and pre-operative Coumadin use (OR, 1.72;  $P=.04$ ), while non-significant factors included use of silver-eluting alginate dressing (OR, 0.91;  $P=.65$ ), nonautogenous conduit use (OR, 0.82;  $P=.47$ ), nonclean classification (OR, 1.72;  $P=.15$ ), and total incision length (OR, 1.01;  $P=.16$ ). Our single institution cost analysis demonstrated a similar WC rate of 27% ( $n=62$ ), of which 64.5% ( $n=40$ ) were SSI. WC were associated with a longer initial length of stay (iLOS; 8.2 v. 6 days;  $P=.0025$ ), higher 30-day readmission rates (23% v. 6%,  $P=.0001$ ), and longer cumulative length of stay (cLOS; 10.1 v. 6.2 days;  $P=.0001$ ) compared to patients with no WC.

The mean total 30-day cost of care was  $\$37,007 \pm 24,084$  Standard Deviation (SD) (total direct costs =  $\$24,838 \pm 15,400$  SD; total indirect cost =  $\$12,189 \pm 9,373$  SD) (Table 1). By bivariate analysis, these total 30-day costs were not significantly different between the subset of patients receiving silver-eluting alginate vs. gauze dressing immediately post-operatively ( $\$38,193 \pm 21,653$  SD v.  $\$36,235 \pm 26,372$  SD;  $P=.0732$ ). The total 30-day costs did not vary significantly according to the site of the lower extremity revascularization ( $P=.1657$ ) (Table 2). The “groin only” procedures in Table 2 were endovascular aneurysm repair (EVAR) procedures, while the remaining procedures in Table 2 were largely reflective of bypass procedures. Due to concerns about device costs in EVAR cases driving cost differences, we also performed a subanalysis on those two groups and found no significant 30-day cost difference between EVAR procedures and bypass procedures (Table 2).

While there was no apparent difference in total 30-day costs according to wound dressing or surgical site, our bivariate analysis comparing WC with NC demonstrated that the mean incremental cost of WC at 30 days was \$11,464, representing costs that were 33.6% higher, on average, for patients with WC than NC ( $\$45,555 \pm 32,386$  SD vs.  $\$34,091 \pm 19,374$  SD;  $P=.0182$ ; Table 3). These increased costs were almost evenly split between direct and indirect costs (\$5,897 and \$5,566, respectively), although only the indirect costs were statistically significantly elevated. Contributors to increased indirect costs included increased length of stay (8.2 vs. 6 days), increased 30-day readmission rates (23% vs. 6%), and their associated costs (eg. lengthier nursing care, etc.). The presence of WC continued to be a significant contributor to total 30-day costs even after accounting for potential confounders by multivariable analysis ( $P=.0037$ ) (Table 4). When accounting for potential confounders, our multivariable generalized linear model (GLM) demonstrated that the mean incremental cost of WC at 30 days was  $\$9,915 \pm 3,375$  standard error (SE),  $P=.0037$ . By multivariable analysis, other factors that contributed significantly to

total 30-day costs included age (on average, increased costs of  $\$320 \pm 142$  SE per year of increased age), estimated blood loss ( $\$7.49 \pm 3.49$  SE per ml of intra-operative blood loss), operative time ( $\$100$  per  $\pm 17.79$  SE per minute of operative time), and incision length ( $-\$215 \pm 77.4$  SE per cm incision length).

For the WC subset, the increased total 30-day costs were also seen in bivariate analysis ( $\$35,448 \pm 20,116$  SD vs.  $\$45,307 \pm 36,522$  SD for no SSI and SSI, respectively; Table 5). These differences were entirely accounted for by indirect costs, including hospital bed and nursing costs ( $\$11,339 \pm 7,964$  SD vs.  $\$16,395 \pm 13,570$  SD,  $P=.0135$ ). Although total 30-day costs did not vary significantly between different procedure types (revascularization vs. endovascular aneurysm repair) by bivariate analysis, the distribution of costs between direct and indirect costs was statistically significant ( $\$23,789 \pm 16,279$  SD vs.  $\$29,689 \pm 10,062$  SD for direct costs and  $\$13,407 \pm 9,851$  SD vs.  $\$7,624 \pm 5,212$  SD for indirect costs, Table 6). The greater indirect costs for revascularization patients represented a longer average LOS.

## DISCUSSION

Our study demonstrates that at a selected tertiary care academic medical center, the mean cost of WC following lower extremity vascular surgeries is \$11,464, or +33.6% of the cost of care for NC, the primary contributors of which are increased LOS, increased readmission rates, and their associated costs (ex. lengthier nursing care, etc.). When controlling for potential confounders by GLM multivariable analysis, the incremental cost remains significant at \$9,915. In addition to the WC, other significant contributors to 30-day post-operative total cost include age, EBL, operative time, and incision length. These findings for age, EBL, and operative time are not surprising given that increasing age and EBL are associated with worse surgical outcomes and greater operative time requiring greater resources.<sup>21</sup> Unlike previous publications suggesting increased SSI rates among groin incisions, our study did not find significant variation in 30-day total costs according to lower extremity anatomic site. This may be due to the study not being adequately powered for this comparison, or different and counterbalancing contributions to cost among the various procedures.

The current findings are relatively consistent with previous single institution and database studies evaluating the extended length of stay and costs associated with WC. We demonstrated an increased 30-day cumulative LOS of 3.9 days and incremental cost of \$11,464 (bivariate) and \$9,915 (multivariable) associated with WC, while Vogel et al. demonstrated a 3.5 day increased LOS and \$11,851 increased costs,<sup>9</sup> Kuy et al. demonstrated a 5.8 day increased LOS,<sup>14</sup> Kirkland et al. demonstrated a 12 day increased LOS and \$5,038 increased costs,<sup>22</sup> Boltz et al. demonstrated a 4.3 increased LOS and \$10,497 increased costs,<sup>11</sup> and Schweizer et al. demonstrated \$11,876 increased costs for SSI.<sup>16</sup> The differences seen in these data may reflect different patient populations and different regional and hospital-specific costs.

Of note, our fiscal results largely differ from those published by Childress et al., a non-concurrent cohort post-operative silver-eluting (Acticoat) dressing study in the VA setting.<sup>23</sup> Childress et al. described a 64% reduction in WC with the use of silver-eluting alginate dressing as well as increased cost-effectiveness with use of the silver-eluting alginate system. Because of the clinical benefit of silver-eluting alginate dressing in the study, the authors were able to calculate that the number needed to treat to prevent one wound infection was 11. The authors subsequently showed that a total \$110 investment in 11 silver alginate dressings would save \$5,595 (their calculated cost of a WC), a very favorable cost-benefit ratio. The discrepancy of results between our study and Childress et al.'s is due to the fact that their non-randomized and non-concurrent report suggested advantages with the dressing, while our subsequent randomized trial failed to show WC benefit.<sup>19</sup> Notably, the direct cost differential between WC and no WC found by Childress et al. (\$5,595) was very close to the differential demonstrated in our study (\$5,897). Furthermore, the incremental LOS for WC patients in the Childress et al. study was much

greater than that seen in our study (16 days vs. 2.2 days), likely reflective of differences between the VA Health System and non-federal hospitals.

Although there is extensive research evaluating the incidence and risk factors for WC following lower extremity vascular procedures, less is known about the total financial burden and cost drivers of post-operative care involving WC. While the primary analysis did not show any health or cost benefit to using silver alginate dressing to reduce WC, this study quantified the incremental costs associated with WC while controlling for patient and procedural factors. This highlights the significant savings that can be achieved through products or quality improvement strategies that either reduce the rate of WC or improve the subsequent treatment of WC. Based on our findings, WC reflect approximately \$10,000 of potential savings. Innovators who develop devices, standardized processes such as checklists, or other interventions that reduce WC rates can use this estimate to judge the financial feasibility of their work (in cost savings or return of investment) before committing significant resources to product development or process improvement, and ultimately capture some of the cost reductions associated with fewer WC.

This study is not without limitations. The parent study was powered for the clinical outcome of WC and this present study may not have been adequately powered to elucidate cost differences for some of the relevant factors. Furthermore, our study population included a heterogeneous group of patients, procedures, and practices that further reduced the analytical specificity. Our cost figures did not include care at outside institutions, non-billable care, or costs to patients, families, and society. While contemporary, our findings may have limited generalizability, since the study was performed at a single tertiary institution. Finally our study took place in a controlled environment with likely increased efforts by the surgeons to minimize wound complications since they knew they were being studied, a phenomenon termed the Hawthorne effect. Therefore, WC rates, and their associated costs, for lower extremity revascularization procedures may be higher than reported in our study. These limitations notwithstanding, our report is among the few to provide detailed incremental costs of vascular WC and highlights the significant potential savings that can be achieved through products or care process quality improvement strategies that either reduce the rate of WC or improve their treatment.

Furthermore, while costs are an important factor in the adoption of new products, cost and cost-effectiveness research is just one, among many, ways to evaluate the usefulness of new innovations. Such analyses cannot completely capture all the short-term and long-term costs and benefits associated with new products and procedures. For example, patient costs due to delayed recovery and impaired work productivity are often overlooked. Additionally, innovation is expensive and incremental, such that iterative improvements to current innovations may result in better efficacy at lower costs over time. Such factors are beyond the scope of this paper but should be considered when designing policies that affect product development and the adoption of technology.

## **CONCLUSIONS**

As healthcare shifts towards a value-based delivery system in which costs and quality play an increasingly important role, the importance of preventing WC to curtail costs and improve outcomes will be increasingly obvious. Although our study did not demonstrate any additional cost-benefit of silver-eluting alginate dressings compared to conventional gauze, significant potential cost savings may be gained from future research and product development that focuses on preventing WC.

## FIGURES

### BIVARIATE COMPARISON OF 30-DAY COSTS WITH ACTICOAT AND GAUZE DRESSING

Total Costs (Acticoat and Gauze pts)		Mean	Median	SD	Min	Max
Total Charge (\$)		134,464	114,437	72,072	43,244	510,382
Total Cost (\$)		37,007	31,125	24,084	8,425	164,070
Total Direct Cost (\$)		24,838	21,654	15,400	5,930	102,383
Total Indirect Cost (\$)		12,169	9,257	9,373	2,494	61,688
Acticoat pts Costs		Mean	Median	SD		
Total Charge (\$)		136,956	12,639	64,554		
Total Cost (\$)		38,193	34,900	21,653		
Total Direct Cost (\$)		25,539	23,346	13,728		
Total Indirect Cost (\$)		12,653	9,683	8,715		
Gauze pts Costs		Mean	Median	SD	Acticoat Mean vs. Gauze Mean	
Total Charge (\$)		133,200	110,230	79,192	Total Charge (\$)	P=.1982
Total Cost (\$)		36,235	29,881	26,372	Total Cost (\$)	P=.0732
Total Direct Cost (\$)		24,421	20,767	16,945	Total Direct Cost (\$)	P=.0968
Total Indirect Cost (\$)		11,813	8,450	10,042	Total Indirect Cost (\$)	P=.0785

**TABLE I.** Total charges and costs for all vascular procedures included in this study, further sub-divided by procedures using silver-eluting Acticoat dressing and gauze dressings. Direct costs include operating room costs, devices, additional procedures, while indirect costs include hospital room and nursing charges.



## COMPARISON OF TOTAL 30-DAY COSTS BY ANATOMIC LOCATION

Procedure Location	Number of procedures (n)	Total Costs (\$)		
		Mean	Median	SD
Supra-inguinal inflow to femoral	18	33,594	33,414	10,902
Femoral-femoral	4	22,273	19,436	10,809
Groin only (EVAR)	82	34139	30770	19969
Femoral above-knee popliteal	17	34982	22702	24976
Femoral below-knee popliteal	31	37960	28385	29327
Femoral tibial/pedal	38	44231	37981	27108
Popliteal tibial/pedal	12	35570	27741	26012
Tibial/pedal	2	68612	68612	72233
Other	23	40826	34729	25770

**TABLE II.** Comparison of total 30-day post-operative costs by lower extremity vascular procedure location.

## COMPARISON OF TOTAL 30-DAY COSTS BY WOUND COMPLICATION STATUS

		Mean	Median	SD		
<b>No WC</b> <b>N=164</b>	<b>Total Charge (\$)</b>	125,722	109,634	58,582		
	<b>Total Cost (\$)</b>	34,091	30,189	19,374		
	<b>Total Direct Cost (\$)</b>	23,362	21,280	12,784		
	<b>Total Indirect Cost (\$)</b>	10,730	8,206	7,578		
<b>WC</b> <b>N=62</b>	<b>Total Charge (\$)</b>	160,187	126,505	95,886	<b>WC vs no WC</b>	<b>Mean Diff (% increase)</b>
	<b>Total Cost (\$)</b>	45,555	35,424	32,386	P=.0169	+34415 (27.4%)
	<b>Total Direct Cost (\$)</b>	29,259	23,487	20,373	P=.0182	+11464 (33.6%)
	<b>Total Indirect Cost (\$)</b>	16,296	12,202	12,240	P=.1186	+5897 (25.2%)
					P<.0001	+5566 (51.2%)

**TABLE III.** Comparison of total 30-day post-operative costs by lower extremity vascular procedure location. WC include superficial surgical site infections, deep surgical site infections, dehiscence, or other (seroma, lymphocele, hematoma, etc.).

# **MULTIVARIABLE ANALYSIS OF CONTRIBUTORS TO TOTAL 30-DAY POST-OPERATIVE COST**

	<b>Parameter Est (\$)</b>	<b>Std Error (\$)</b>	<b>P value (\$)</b>
<b>Intercept</b>	12,101	15,751	.4432
<b>Acticoat vs. Gauze</b>	2,946	28,230	.2977
<b>WC vs. no WC</b>	9,915	3,375	.0037
<b>EVAR vs revasc</b>	1,846	3,966	.642
<b>Age (yrs)</b>	320	142	.0259
<b>Female vs male</b>	2,502	3,048	.4127
<b>Race</b>			
<b>White</b>	-10,316	6,867	.1345
<b>Black</b>	959	8,847	.9137
<b>EBL (ml)</b>	7.49	3.49	.0329
<b>Operative time (min)</b>	100	17.79	<.0001
<b>Incision length (cm)</b>	-215	77.4	.0059

**TABLE IV.** Generalized linear model (GLM) multivariate analysis of factors contributing to total 30-day post-operative cost. The "parameter est" reflects the calculated beta value for each variable in the model.

## **COMPARISON OF TOTAL 30-DAY COSTS BY SURGICAL SITE INFECTION STATUS**

	<b>Mean</b>	<b>Median</b>	<b>SD</b>	
<b>Total Charge (\$)</b>	128,978	114,001	59,415	
<b>Total Cost (\$)</b>	35,448	30,857	20,116	
<b>Total Direct Cost (\$)</b>	24,108	21,908	13,062	
<b>Total Indirect Cost (\$)</b>	11,339	9,035	7,964	
				<b>SSI vs no SSI</b>
<b>Total Charge (\$)</b>	163,150	122,560	110,105	P=.2530
<b>Total Cost (\$)</b>	45,307	33,340	36,522	P=.4502
<b>Total Direct Cost (\$)</b>	28,912	21,039	23,105	P=.9726
<b>Total Indirect Cost (\$)</b>	16,395	11,422	13,570	P=.1035

**TABLE V.** Comparison of total 30-day post-operative costs by surgical site infection status. An SSI is any WC in which there was localized redness, heat, swelling, and pain, according to the CDC criteria.

# COMPARISON OF TOTAL 30-DAY COSTS BY TYPE OF PROCEDURE

		Mean	Median	SD	
<b>Revascularization</b> <b>N=181</b>	<b>Total Charge (\$)</b>	136,758	114,437	77,304	
	<b>Total Cost (\$)</b>	37,196	30,242	26,019	
	<b>Total Direct Cost (\$)</b>	23,789	19,820	16,279	
	<b>Total Indirect Cost (\$)</b>	13,407	10,483	9,851	
<b>EVAR</b> <b>N=46</b>	<b>Total Charge (\$)</b>	132,445	115,158	46,672	<b>Revasc vs EVAR</b>
	<b>Total Cost (\$)</b>	37,306	32,939	14,324	P=.3464
	<b>Total Direct Cost (\$)</b>	29,682	26,772	10,062	P=.0588
	<b>Total Indirect Cost (\$)</b>	7,624	6,718	5,212	P<.0001

**TABLE VI.** Comparison of total 30-day post-operative costs by type of vascular procedure (revascularization vs. EVAR).

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## **PERCUTANEOUS INTERVENTIONS FOR CARDIAC VALVULAR DISEASE: A REVIEW OF CONTEMPORARY PRACTICES AND FUTURE DIRECTIONS**

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### **Abstract**

Open-heart surgery has been the mainstay of management of symptomatic valvular disease since the 1960s, when mechanical valves were first utilized for surgical repair of native, aortic and mitral valves. Within the last decade, these practices have been challenged with the innovative use of percutaneous transcatheter approaches for treatment of various valvular pathologies. There have been significant advances among these percutaneous valve technologies, especially in the context of aortic valve replacement, with comparable patient outcomes to the conventional open sternotomies in high and intermediate risk patients. With increased interest among clinicians to develop best practices for management of valvular disease, more emphasis is placed on multi-disciplinary approaches to patient care including the surgeons. As we continue to adopt and gain experiences with newer approaches to patient management, it becomes increasingly relevant and appropriate to weigh the risks and benefits of various contemporary practices to help guide clinical decisions. This evidence-based assessment of existing technological platforms is pivotal to avoid unnecessary waste of resources, reduce costs and improve overall patient survival in this global economy. In this chapter, we will dissect and analyze various contemporary percutaneous technologies for the management of valvular heart disease. Specifically, we will examine the effectiveness, trends, and outcomes of transcatheter approaches for aortic (TAVR) and mitral valve (TMVR) replacement. We will also elucidate the utility of various emerging balloon valvuloplasty techniques, MitraClip, and valve-in-valve approaches. Understanding the limitations of these current technologies will hopefully help identify new avenues for research and innovation.

**Keywords:** TAVR, TMVR

## Introduction

Surgical valve replacement with open-heart surgery has been the mainstay of treatment for valvular disease since it was first pioneered a half-century ago. In 1954, Hufnagel et al. described the first use of ball-and-cage technology in the descending thoracic aorta to treat aortic insufficiency.<sup>1</sup> In 1960, Braunwald performed the first successful mitral valve replacement while Harken performed the first successful aortic valve replacement.<sup>2,3</sup> Since that time, open surgical techniques have evolved with the adoption and enhancement of new technologies, including bioprosthetic valves, resulting in significant improvements in patient outcomes following surgery for valvular disease. In fact, for many valvular pathologies, such as aortic stenosis, valve replacement has been shown to be a superior and viable treatment strategy compared to medical therapies alone.<sup>4,5 6 7 8</sup>

Unfortunately, a substantial number of patients, especially the frail and elderly, remain poor surgical candidates for open valve replacement, and previously were not offered surgery due to their high-risk status.<sup>9</sup> With limited options available for definitive management, the prognosis for these patients was grim until the past decade. Within the last 15 years, however, there have been significant advancements and innovations in less invasive, catheter-based technologies that offer alternative options for treatment in previously inoperable or high-surgical-risk patients. By avoiding cardiopulmonary bypass in most cases, decreasing overall operative time, avoiding the use of either cardioplegia, full sternotomies, or other physiologic stresses associated with open-heart surgery, transcatheter valve therapies have emerged with promising short and mid-term results.<sup>10,11</sup>

Henning Rud Andersen first began experimenting with transcatheter aortic valves in pigs in the 1980s.<sup>12</sup> Unfortunately, the size of the system precluded application in humans. In 2000, using a bovine vein valve sewn into a platinum/iridium stent, Bonhoeffer et al. performed the first transcatheter valve replacement, replacing the pulmonary valve in a tetralogy of Fallot patient with prosthetic conduit pulmonary stenosis.<sup>13</sup> Subsequently, in 2002, without the use of echo imaging, Cribier et al. performed the first transcatheter aortic valve replacement (TAVR) using a femoral vein and transseptal approach in a 57-year-old gentleman with a calcified bicuspid aortic valve.<sup>14</sup> The TAVR was successfully placed with hemodynamic improvement sustained for 4 months, with moderate stable paravalvular regurgitation, but, due to noncardiac complications of leg ischemia and subsequent infection, the patient died 17 weeks after the procedure. Soon after, other clinicians began experimenting with transapical and transfemoral TAVR approaches, although many of these experiences were accompanied by fairly high mortality and stroke rates.<sup>15</sup> Initial data from the Initial Registry of Endovascular Implantation Of Valve in Europe (I-

REVIVE) and Registry of Endovascular Critical Aortic Stenosis Treatment trial (RECAST) registries, as well as the Edwards REVIVAL trial, demonstrated feasibility for transcatheter valvular procedures and laid the groundwork for larger subsequent trials and technological advancements.<sup>16 15</sup> Some of these landmark studies include the PARTNER (2010),<sup>11 17 18 19</sup> PARTNER 2 (2011),<sup>10 20 5</sup> CoreValve US Pivotal Trial (2014),<sup>21</sup> and more recently the SURTAVI trial (2017).<sup>22</sup>

## **Aortic Valve Replacement**

The most significant technological advancements and largest clinical successes with transcatheter therapies have been observed with transcatheter treatment of aortic stenosis. This success has been primarily due to the relative ease of access to the aortic valve through the retrograde, or transfemoral approach, and due to Edwards Lifesciences (Irvine, CA) early technological success in navigating the aortic arch with endovascular approaches.<sup>23</sup>

Aortic stenosis (AS), if untreated, is a fatal diagnosis, with a prognosis of 2 to 5 years depending on symptom severity.<sup>24</sup> Although aortic valve replacement (AVR) is the only effective therapy, approximately one-quarter to one-third of AS patients are not offered surgical treatment options due to their poor surgical candidacy, secondary to comorbidities or underlying cardiac function.<sup>25 9</sup> While balloon aortic valvuloplasty (BAV) was offered to some of these patients in the past, BAV efficacy was severely limited by early recurrence of stenosis and contraindication in patients with aortic regurgitation.<sup>26 27</sup> Patient risk stratification tools such as the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) and EuroSCORE II are most commonly utilized to help identify inoperable and poor surgical candidates.<sup>28</sup> In contrast to AS, for which annular calcification provides a landing zone for transcatheter aortic valve placement, aortic regurgitation (AR) has proven less amenable to treatment by transcatheter aortic valve replacement (TAVR) due to the absence of a rigid aortic landing zone.<sup>29</sup>

## **Current TAVR Technologies and Clinical Evidence**

There are two commercially available TAVR technologies approved by the Food and Drug Administration (FDA): the balloon-expandable Edwards SAPIEN system (Edwards Lifesciences Corporation; Irvine, CA) and the self-expandable Medtronic CoreValve system (Medtronic, Inc.; Minneapolis, MN).<sup>30</sup> Several recent landmark studies examining TAVR technologies have emerged, challenging current treatment guidelines. These include the Placement of Aortic Transcatheter Valves



(PARTNER) trials, as well as the CoreValve Pivotal High Risk and Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI) trials.

The Placement of AoRTic TraNscathetER Valve Trial (PARTNER trial) was a multicenter, randomized controlled trial that demonstrated the efficacy of the SAPIEN system relative to medical and open surgical management. The Edwards SAPIEN system is a balloon-expandable, trileaflet, bovine pericardial valve sewn into a stainless steel frame.<sup>30</sup> The newer SAPIEN 3 system is a modification of the second-generation SAPIEN XT valve, with an added polyethylene terephthalate outer skirt, Cobalt Chromium frame, lower profile, and lower frame height to reduce paravalvular leaks, vascular complications, and coronary occlusion, respectively.

The PARTNER A cohort investigated TAVR (SAPIEN) versus SAVR in high-risk patients with symptomatic severe AS and demonstrated comparable mortality rates at 30-days, extending out to 5-years.<sup>10 20 5</sup> Whereas TAVR was associated with higher 30-days stroke and TIA rates, these differences were non-significant at 5-years. Although TAVR was associated with more vascular complications and paravalvular leak at 30-days than SAVR, TAVR patients had clinically significant improvement in symptoms, including decreased incidence of major bleeding and new-onset atrial fibrillation at 30-days. PARTNER B cohort investigated transfemoral TAVR versus medical management (including balloon aortic valvotomy) in patients with severe AS who were deemed inoperable surgically. The investigators found a reduced one-year mortality rate (30.7% vs. 50.7%) and improved New York Heart Association (NYHA) functional class in the TAVR group relative to the medical management group.<sup>11 17 18 19</sup>

Although the 30-day stroke risk was higher in the TAVR group than the control (6.7% vs. 1.7%), there was no notable difference by 5 years.

The PARTNER 2A trial investigated TAVR (SAPIEN XT) versus SAVR in intermediate-risk patients with symptomatic severe AS, including both transfemoral and transapical approach patients. At 2 years, the mortality and major stroke rates were comparable between the two groups. Moreover, mortality and major stroke rate was less among the transfemoral access TAVR patient subset than the SAVR group (17% vs. 20%;  $P=0.05$ ), while the rates were similar between the transthoracic access TAVR patient subset and SAVR group.<sup>31</sup> Consistent with the PARTNER A cohort results, TAVR patients had larger aortic valve areas and experienced less episodes of acute kidney injury (AKI), major bleeding, and new onset atrial fibrillation, while SAVR patients experienced less paravalvular leaks and fewer vascular complications. A propensity-matched study comparing SAPIEN 3 with SAVR among intermediate-risk patients found that TAVR was superior relative to SAVR with regards to mortality, strokes, and moderate or severe AR at 1-year.<sup>32</sup> Enrollment is currently ongoing for SAPIEN TAVR versus SAVR for low-risk surgical patients (PARTNER 3 trial).

The Medtronic CoreValve system, on the other hand, includes a self-expandable nitinol frame with a sewn-in trileaflet, porcine pericardial valve. The second generation Evolut R valve is a modification of the first generation CoreValve, and has the added capability of being repositionable and recapturable once two-thirds of the valve is deployed. In 2017, the FDA approved the newest Evolut PRO valve for high or extreme-surgical risk patients, a valve which has additional design features to reduce paravalvular leak. As discussed below, the CoreValve system has already demonstrated non-inferiority to surgical aortic valve replacement (SAVR) for high-risk and intermediate-risk patients, and is currently under investigation for indications for low-risk patients.

In parallel to the PARTNER Cohort B study, the CoreValve Extreme Risk United States Pivotal Trial demonstrated the efficacy of the CoreValve relative to medical management for inoperable patients with AS. This prospective single-arm study compared the CoreValve to a pre-specified mortality estimate of medical management, with the CoreValve demonstrating a much lower mortality rate (26% vs. 43%).<sup>21</sup>

In contrast to the PARTNER A cohort, the United States CoreValve High Risk Study comparing Medtronic's self-expanding CoreValve to SAVR demonstrated lower 1- and 2-year mortality among TAVR patients than SAVR patients (14.2% vs. 19.1%,  $P=0.04$ , and 22.2% vs. 28.6%,  $p<0.05$ , at 1- and 2-years, respectively).<sup>33 34</sup> TAVR was associated with more frequent vascular complications and permanent pacemaker implantation than SAVR, whereas SAVR was associated with more major bleeding and AKI. The SURTAVI trial was a randomized controlled trial comparing the CoreValve system (both the CoreValve and Evolut R valves) to SAVR in intermediate-risk patients. At 2-years, the mortality and stroke rates between the two groups were similar.<sup>22</sup> Enrollment is currently ongoing for CoreValve TAVR versus SAVR for low-risk surgical patients. The NOTION trial was a small European randomized-controlled trial comparing the CoreValve system to SAVR among low-risk patients.<sup>35</sup> Composite death and stroke rates were similar between the two groups at 2 years (16% vs. 19% for TAVR and SAVR, respectively), while TAVR patients had more improvement in effective orifice area but more frequently required permanent pacemaker implantation (PPI) and experienced more aortic regurgitation (paravalvular leak).<sup>36</sup> Nonetheless, the results of this trial were inadequate to guide future clinical decisions given the small sample size and non-homogenous patient cohort.

Moreover, there is insufficient evidence to definitely guide preference of one TAVR valve over another. The CHOICE trial was the only randomized-controlled trial to compare the SAPIEN and CoreValve technologies. Although operative success was higher with the SAPIEN group than the CoreValve group, clinical outcomes at 1-year were equivalent.<sup>37 38</sup> Unfortunately, these results are now largely irrelevant since the CHOICE trial compared Edwards' and Medtronic's first-generation technologies, both which have now been replaced by newer and relatively better valve technologies.

For both the SAPIEN and CoreValve systems, very long-term outcomes are still lacking despite the promising short-term outcomes. As market competition persists, these valve technologies will inevitably continue to evolve and improve, addressing patient and device-related issues that were previously seen. Nonetheless, there is an increasing body of literature demonstrating the efficacy of TAVR in high and intermediate risk patients, with widespread utilization observed in many patient populations, including the elderly. The 2016 Society of Thoracic Surgeons/American College of Cardiology (STS/ACC) Transcatheter Valve Therapy (TVT) Registry demonstrated that the annual volume of TAVR procedures performed has increased from 4,627 in 2012 to 24,808 in 2015. The volume will inevitably continue to grow, demanding that cardiac specialists become more familiar with the procedures.<sup>39</sup>

### **TAVR in Clinical Practice**

Based on promising results of the above trials, the FDA approved the Edwards SAPIEN in 2011, SAPIEN XT in 2014, SAPIEN 3 in 2015, Medtronic CoreValve in 2014, Evolut R in 2015, and Evolut PRO in 2017 for high-risk surgical patients with AS. The CoreValve, SAPIEN XT, and SAPIEN 3 were also recently approved for valve-in-valve operations in high-risk surgical patients with a prior failed bioprosthetic valve (discussed later on in this chapter). The SAPIEN XT, SAPIEN 3, and Evolut systems have also been approved for intermediate-risk patients. In 2014 the American College of Cardiology (ACC) and American Heart Association (AHA) issued new consensus recommendations for the management of aortic stenosis. Based on these guidelines, surgical AVR is recommended in patients who meet an indication for AVR with low or intermediate risk (Class I, level of evidence A). Likewise, TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR and who have high surgical risk (Class IIA, level of evidence B).<sup>40</sup> Moreover, recent randomized trials and clinical registries have failed to demonstrate widespread, clinically relevant differences in outcomes between the SAPIEN and CoreValve systems. As a consequence, deciding on which valve to use is often based on patient-specific and center-specific considerations, with increasing variability among institutions. For instance, CoreValve is preferred in patients with a borderline iliac diameter (5mm) due to the valve's profile, and in patients with low ejection fraction in order to avoid rapid ventricular pacing. Importantly, clinicians must also utilize the EuroSCORE II and STS-PROM risk scores in risk-stratifying patients appropriately, although these scores fail to take into account cirrhosis, extent of coronary artery disease, frailty and functional capacity of individuals. Thus, a multi-disciplinary team approach is essential and perhaps mandatory in order to improve patient selection, and outcomes. This fact is particularly relevant among the elderly patients i.e. those above 80 years, where multiple comorbidities can complicate perioperative management. Although initial TAVR experiences used both transfemoral

and transthoracic or transapical approaches, the transfemoral approach is now widely favored due to a lower mortality rate.<sup>41 42</sup> Nonetheless, for patients for whom a femoral approach is not an option due to vascular or anatomic abnormalities, alternative approaches, including subclavian, direct aortic, transapical, and transcarotid, are possible.

With continuous improvement in TAVR technologies and increasing operator experiences, the number of complications associated with TAVR has decreased significantly in recent years. Innovations in valve technologies have also contributed towards this improvement. More notable complications can be categorized as bleeding and access-related complications, valve-related complications, and complications to other organ systems. As previously highlighted, TAVR has been shown to have a relatively smaller operative mortality, less incidence of AKI and new onset atrial fibrillation, and fewer bleeding complications. However, TAVR is associated with higher rates of re-intervention, permanent pacemaker implantation, and aortic regurgitation.<sup>31,32,43,44</sup> Although TAVR poses a relatively small risk of coronary obstruction with native aortic valves, this risk increases approximately four-fold with valve-in-valve operations (0.7% vs 3.5%).<sup>45</sup> Atrioventricular conduction abnormalities, requiring a new pacemaker or intracardiac defibrillator, are post-operatively observed in approximately 8.8% of patients. Although the SAPIEN valve traditionally had lower PPM implantation rates than the CoreValve system, the outer skirt of the SAPIEN 3 valve, meant to reduce rates of paravalvular leak, has increased PPI rates to 10.2% with that valve.<sup>46</sup> Moderate to severe paravalvular regurgitation, which is observed in 0-24% of TAVR patients, is associated with higher 30-day and 1-year mortality rates.

Likewise, in the PARTNER trial, the 30-day stroke or transient ischemic attacks (TIA) was 3.3%, and was associated with increased mortality.<sup>47</sup> In the CoreValve trials, the stroke or TIA rate was 8.4% by year 1.<sup>48</sup> With observations of larger retrospective studies, stroke rate consistently varies between 2-5%, with similar rates among all valve types. While these rates reflect overt stroke rates, the Sentinel randomized-controlled trial of embolic protection devices suggests that MRI evidence of subclinical cerebral lesions occurs in upwards of 90% of TAVR patients.<sup>49</sup> While the clinical relevance of these imaging lesions has yet to be fully determined, the SENTINEL trial found that while the Sentinel embolic protection device (Claret Medical; Santa Rosa, CA) is safe and captured debris in 99% of patients, leading to a net reduction in lesion volumes post-operatively on MRI, the Sentinel device was not associated with any difference in neurocognitive function relative to the control group without embolic protection.<sup>50</sup> In contrast to these findings, a meta-analysis of four smaller studies suggested an improved cognitive function was observed with the use of embolic protection devices, although the rate of overt strokes and deaths remained unchanged.<sup>51</sup> These complication rates will likely change as indications for TAVR expand to new groups, including low-risk patients, and as market competition drives new entrants and technological innovation in the field. Among such competitors is the LOTUS Edge valve (Boston

Scientific Corporation; Natick, MA), a fully repositionable and retrievable device, which has demonstrated promising results in the Italian RELEVANT study.<sup>52</sup>

## **Mitral Valve Repair and Replacement**

Catheter-based interventions to treat mitral stenosis and mitral regurgitation have progressed much more slowly than for aortic stenosis. This relatively slow progress is not due to a small disease burden—mitral regurgitation affects approximately 10% of individuals above the age of 75.<sup>24</sup> Instead, new mitral interventions are slowed by the complex anatomy and valve-delivery challenges associated with the mitral valve. Such challenges include the mitral valve's elliptical, saddle shape; asymmetric leaflets; apposition to the left ventricular outflow tract and aortic valve; interpatient variation of the aortomitral angle; the subvalvular mitral apparatus; the heterogeneity of mitral valve disease; and the difficult transseptal approach and angle, which has limited many technologies to a transapical approach.<sup>53 54 55</sup> Similarly to aortic valve disease, many patients with mitral disease are not referred for surgical treatment.<sup>56</sup> Many patients with mitral disease have comorbidities that pose prohibitively high surgical risks. Furthermore, mitral valve disease is heterogeneous—while the preferred treatment for primary degenerative mitral regurgitation (MR) has been surgical repair, there is less certainty around management of secondary functional MR. For patients for whom open surgical mitral repair has not been a feasible option, mitral valve replacement has been the treatment of choice.<sup>56</sup> Catheter-based techniques would offer potential treatment alternatives for previously inoperable patients and, like for the aortic valve, with further technological advancements could even improve treatments for open surgical candidates. As detailed below, many of the catheter-based mitral repair and replacement technologies, in fact, emulate established surgical techniques, which have been very effective in managing both mitral stenosis and regurgitation.

### **Mitral Balloon Valvuloplasty**

Although the prevalence has decreased in the United States and Europe, mitral stenosis (MS) continues to be predominantly caused by rheumatic fever, which leads to mitral leaflet thickening, commissural fusion, and chordal dysfunction.<sup>57</sup> Other causes of mitral stenosis include mitral annular calcification (MAC), mitral bioprosthesis dysfunction, and post-commisurotomy restenosis. The first successful mitral valve repair was performed by Dr. Elliot Cutler at Brigham and Women's Hospital in 1923; Cutler performed a blind mitral commissurotomy on a young girl with rheumatic mitral stenosis.<sup>58</sup> While MS had been traditionally successfully managed with open and closed surgical mitral commissurotomy, in the early 1980s, Inoue in Japan

and Lock in India pioneered the use of a percutaneous, inflated balloon made of rubber to treat the disorder.<sup>59</sup>

<sup>60</sup> Although percutaneous mitral balloon valvuloplasty (PMBV) is not a suitable treatment strategy for all causes of MS, such as MS secondary to MAC, Inoue's single balloon technique has since become the preferred method of treating rheumatic MS in select patients.<sup>61 57</sup>

PMBV works by fracturing calcified commissures. During the procedure, the balloon catheter is advanced into the left atrium via a transseptal approach and passed across the stenotic mitral valve. The Inoue balloon, which has 3 distinct portions with varying compliance, is inflated and rapidly deflated to fracture the commissures, mimicking surgical commissurotomy.<sup>62</sup>

A detailed discussion of patient selection and indications for, and complications of, PMBV is beyond the scope of this chapter. In brief, patient selection is based on patient symptoms and anatomy, which can be assessed using the Wilkins score that evaluates a combination of variables including valve calcification, mobility, thickening, and the subvalvular apparatus.<sup>63</sup> Major complications include hemopericardium and MR.<sup>64</sup> The limitations of PMBV are the presence of MR and the Wilkins score, so many patients are not indicated except for early rheumatic disease.

The procedure produces excellent short-term valve area and hemodynamic outcomes.<sup>65</sup> Relative to surgical commissurotomy, PMBV has shown comparable results for relieving MS and for subsequent restenosis.<sup>66 67</sup> Most patients' post-procedural valves have an area at least 1.50 cm<sup>2</sup> with minimal or mild MR, which results in improved hemodynamic pressures and gradients, an increase in cardiac output, and significant symptomatic improvement.<sup>57 65</sup> Pulmonary artery pressures and cardiac output continue to improve for at least 1 year, but with time the effective mitral orifice area decreases and the need for reintervention, either surgical or PMBV, increases.<sup>68 69</sup> Nonetheless, upwards of ½ of patients can avoid reintervention for up to 20 years.<sup>70</sup>

## Transcatheter Mitral Valve Repair

While transcatheter interventions technologies have been available for MS for decades, they are much newer avenues for management of MR, which is much more prevalent in the United States than MS (1.7% of population vs. 0.1%).<sup>24</sup> The preferred treatment for primary degenerative MR has been mitral valve repair, which better maintains the subvalvular apparatus and, thus, left ventricular function better than does mitral valve replacement.<sup>71</sup> The only FDA-approved device for transcatheter mitral valve repair is the MitraClip system (Abbott Vascular; Santa Clara, CA), while the Cardioband (Edwards Lifesciences; Irvine, CA) and Carillon (Cardiac Dimensions; Kirkland, WA) mitral systems have received CE Mark approval.

By using a cobalt-chromium clip with two arms that open and close to capture and appose the anterior and posterior mitral leaflets, the MitraClip mimics edge-to-edge mitral repair using an Alfieri stitch and creates a double-orifice mitral valve.<sup>72</sup> The MitraClip was evaluated through the Endovascular Valve

Edge-to-Edge Repair (EVEREST II) trial, which randomized patients with at least moderate to severe MR to either receive a MitraClip or undergo surgical intervention (repair or replacement).<sup>73</sup> At 12 months, 55% of the percutaneous group achieved the primary end point for efficacy (freedom from death, re-operation for mitral dysfunction, and 3+ or 4+ mitral regurgitation) while 73% of the surgical group did, largely due to the higher rate of re-operation for valve dysfunction in the percutaneous group (20% vs. 2%). Although MitraClip is, thus, less effective at reducing MR than surgery and more often required re-operation, patients in the percutaneous group notably had fewer major adverse events at 30 days (15% vs. 48%) and experienced similar benefits with regards to left ventricular size, left ventricular function, and quality of life. At 5 years, the primary endpoint was achieved by 44.2% of the percutaneous arm and 64.3% of the surgical arm, reflecting an increased rate of 3+ or 4+ MR and increased re-operation rates (12.3% vs 1.8%; 27.9% vs. 8.9%, respectively) in the percutaneous arm. The comparison of the 12 month and 5 year data suggests that while MR and re-operation are more common in the percutaneous group, these events are mainly seen within the first year, and the MitraClip is comparably durable to surgery in years 1 to 5.<sup>74 75</sup> The MitraClip is thus approved for patients with moderate or severe primary MR who are at high surgical risk or not considered to be surgical candidates.

Unlike in the United States, MitraClip has been approved for secondary MR in Europe.<sup>76</sup> Observational studies suggest that MitraClip may also demonstrate some efficacy for secondary functional MR.<sup>77</sup> A secondary analysis of the subset of EVEREST II patients with functional MR suggests that these patients may derive relatively more benefit from a MitraClip compared to surgery than do primary MR patients.<sup>74</sup> The Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) Trial is an ongoing randomized controlled trial in the U.S. comparing the MitraClip with medical management for patients with moderate-to-severe or severe functional MR.

As noted earlier, besides the MitraClip, no other devices have yet received FDA approval for percutaneous mitral valve repair. Nonetheless, a few devices, discussed below, have received CE mark approval, and a number of others are undergoing feasibility studies. Percutaneous annuloplasty devices can be categorized as direct, indirect, or apical tethering.<sup>76</sup> The Cardioband system (Edwards Lifesciences; Irvine, CA) is a direct annuloplasty device that mimics surgical repair with an annuloplasty ring by percutaneously attaching an annuloplasty band to the posterior mitral annulus using sutureless screw-in anchors.<sup>78</sup> The Mitralign system (Mitralign; Tewksbury, MA), another direct device, uses two pledgeted sutures to shorten the mitral annular diameter, mimicking the commisuroplasty, and is currently undergoing a feasibility study.<sup>79</sup> Indirect repair systems aim to reduce mitral annular circumference and improve leaflet coaptation through devices placed in the coronary sinus. The Carillon Mitral Contour System (Cardiac Dimensions; Kirkland, WA) is the only CE mark approved indirect device. The system

works by using proximal and distal nitinol anchors that are connected by a nitinol wire; when placed into the coronary sinus, they reconfigure the mitral annulus and narrow the diameter. The Carillon system has been studied in the AMADEUS, TITAN, and TITAN II trials, with promising technical success and functional results.<sup>80 81 82</sup> Finally, the Neochord system (Neochord; Minneapolis, MN) is an CE mark approved apical tetherin device that uses an artificial chord via a transapical approach to connect the posterior mitral leaflet with LV myocardium.<sup>83</sup> All of these devices need further clinical trials and none have gained widespread clinical acceptance.

## Transcatheter Mitral Valve Replacement

As noted above, because of the technical difficulty of percutaneous manipulation of the mitral valve, transcatheter mitral valve replacement (TMVR) therapies have lagged TAVR and mitral repair techniques.<sup>53</sup> Nonetheless, some progress has been made with the use of compassionate SAPIEN TAVR devices to treat failure of surgical mitral bioprostheses in surgically high-risk patients.<sup>84</sup> In a recent case series, all 23 reported patients had successful valve-in-valve implantation with functional improvement to NYHA class I or II at median follow-up of 753 days.<sup>84</sup>

The previously implanted bioprosthetic valves in the aforementioned patients allowed for a landing zone for the balloon-inflatable SAPIEN valves. Since a similar rigid annular structure is created by the presence of severe mitral annular calcification, TMVR using compassionate aortic balloon-expandable valves has been used and reported in the MAC Global Registry.<sup>61</sup> Among the 64 patients reported, the authors demonstrated feasibility of TMVR using SAPIEN valves with a technical success rate of 72%, limited by the need for a second valve in 17.2% of patients. Nonetheless, significant adverse events were observed, with 30-day all-cause mortality rates of 29.7% and LVOT obstruction in 9.3% of patients. For survivors, 84% experienced functional improvement to NYHA I or II at 30 days. The Mitral Implantation of TRANscatheter vaLves (MITRAL) trial is an ongoing trial to study the use of SAPIEN valves for treating inoperable patients with severe MAC or failed surgical rings or bioprostheses.

TMVR in non-calcified mitral valves is more difficult due to lack of a suitable “landing zone.”

Nonetheless, early feasibility studies are ongoing for a number of devices: the Fortis valve (Edwards Lifesciences; Irvine, CA)<sup>85</sup>, the Tendyne Bioprosthetic Mitral Valve System (Tendyne Holdings; Roseville, MN)<sup>86</sup>, the CardiaAQ-Edwards system (Edwards Lifesciences; Irvine, CA)<sup>87,88</sup>, the Tiara system (Neovasc Inc.; Richmond, BC, Canada)<sup>89</sup>, and the Intrepid Twelve system (Medtronic; Minneapolis, MN)<sup>90</sup>. These devices use different techniques for capturing the native mitral leaflets within the device and for securing attachment to the left ventricle. Whether these systems will have a significant long-term clinical impact remains to be seen.



Among the most promising of the TMVR systems is the Tendyne valve, recently investigated in the largest study to date of TMVR.<sup>91</sup> The system design involves an outer D-shape to match the unique mitral annular contour, along with a sealing cuff and polyethylene tether that anchors the Tendyne system to an apical pericardial pad.<sup>92</sup> Mueller et al. treated 30 patients who had severe or moderate-to-severe MR and mean STS predicted 30-day mortality of 7.3%. The Tendyne system was successfully implanted via a transapical approach in 28 patients, all except 1 of whom had Grade 0 MR after the procedure, with an 83% freedom from major adverse events at 30 days. Although this is a promising first step, larger studies need to be conducted.

## **Pulmonary Valve Replacement**

In 2000, the pulmonary valve was the first valve to be replaced using transcatheter technology in a human and, in 2006, the Melody transcatheter pulmonary valve (Medtronic; Minneapolis, MN) became the first commercially available transcatheter valve.<sup>13</sup> Pulmonary valve intervention is indicated for stenosis or regurgitation of prosthetic conduits in patients with congenital heart disease. Patients with congenital heart diseases such as tetralogy of Fallot, truncus arteriosus, or transposition of the great arteries require surgical reconstruction of the right ventricular outflow tract (RVOT) using prosthetic conduits between the RV and pulmonary arteries. Since these conduits do not grow with the patient and often undergo dysfunction (stenosis or regurgitation) with time that impairs RV function, these patients often require re-intervention at some point during adulthood. In order to avoid multiple open surgical re-interventions in these patients, the benefits of a transcatheter pulmonary valve replacement (TPVR) are obvious. Unfortunately, the challenges to percutaneous intervention are extensive, namely dealing with the anatomic variation between patients with different, previously constructed RVOT conduits.

The Melody TPV is a balloon-expandable stent with a sewn in valved bovine jugular venous graft. It is FDA approved for pediatric and adult patients with a dysfunctional RVOT conduit and for failed surgical bioprosthetic pulmonary valves. The Melody TPV has demonstrated effectiveness in management of both pulmonary obstruction and regurgitation, with additional improvements in tricuspid regurgitation.<sup>93-96</sup> The Sapien XT system is also approved for congenital pulmonary valve replacement. Still, the vast majority of patients who need pulmonary valve intervention do not have a conduit and must undergo open-heart surgery. Studies of the feasibility and efficacy of Melody placement in native right ventricular outflow tracts are currently ongoing.

## **Tricuspid Valve Repair and Replacement**

Tricuspid valve disease most often presents as tricuspid regurgitation secondary to left-sided disease, with operative repair or replacement often occurring simultaneously during left-sided valve surgery. Although previously often ignored as likely to resolve with correction of left-sided disease, TR has been shown to negatively impact outcomes, which has led to increased tricuspid operations.<sup>71,97,98</sup> Open tricuspid repairs are effective in improving RV function and reducing mortality, while replacements tend to be limited to those patients for whom repairs are unfavorable. Unfortunately, isolated tricuspid re-operations are associated with high mortality rates, and the number of patients re-presenting with degeneration of a previous tricuspid repair is not insignificant.<sup>99-102</sup> Therefore, there is an opportunity for significant clinical benefits brought about by transcatheter tricuspid repairs and replacements.

Clinical examples of transcatheter tricuspid valve replacement (TTVR) are limited. Just like for TMVR, early reports of tricuspid valve-in-valve transcatheter tricuspid valve replacement (TTVR) have been reported using both Melody and SAPIEN valves.<sup>103-106</sup> There have been fewer valve-in-ring reports published.<sup>107,108</sup> These examples are limited to very high-risk surgical patients, with the previously placed valve or ring providing fluoroscopic landmarks for proper TTVR placement. Preliminary results suggest NYHA functional class improvements of at least 1 grade among patients, but not without complications, including paravalvular leak especially with valve-in-ring procedures.<sup>109</sup>

The first report of a TTVR in a native valve was published by Kefer et al. using a SAPIEN valve via the transfemoral approach for tricuspid stenosis.<sup>110</sup> To provide a landing zone, two covered CP Stents were placed prior to TTVR deployment. After implantation of two valves, the patient's stenosis resolved, with minimal residual TR. Clinical trials are warranted with this device strategy to further substantiate these initial results.

MitraClip has also recently been used to treat severe TR in non-operative patients. In 2016, Schofer et al. published the first use of MitraClip to successfully treat severe functional TR.<sup>111</sup> More recently, Nickenig et al. published a larger series with 97% successful implantation and only 13% of patients experiencing persistent severe TR post-operatively.<sup>112</sup>

Two bicuspidization systems have demonstrated preliminary feasibility for treating TR in native tricuspid valves—the Mitralign system introduced above (known as TriAlign when modified for the tricuspid valve) for the mitral valve, and the TriCinch system (4TECH Cardio Ltd; Galway, Ireland). As discussed above, the TriAlign system uses pledgeted sutures to mimic the surgical Kay procedure, placating the tricuspid annulus along the border of the posterior leaflet, obliterating it.<sup>113 114</sup> The TriCinch system uses a corkscrew implanted near the anteroposterior (AP) commissure to draw the AP commissure towards a stent placed in the IVC, thus reducing the AP tricuspid annulus diameter.<sup>115</sup> These systems are both in their very early stages with feasibility trials and have only demonstrated moderate reductions in TR.<sup>113</sup>

<sup>114-116</sup>Other technologies are also currently under development.<sup>117,118</sup>

## Evolving Indications for Transcatheter Therapies

As centers continue to gain experience using TAVR, and as patients with previously implanted SAVR and TAVR bioprosthetic valves begin to experience valve degeneration or dysfunction, indications for TAVR will continue to expand. Furthermore, as noted above for the development of new mitral, pulmonary, and tricuspid technologies, transcatheter repair systems and valves may soon have a bigger clinical impact for these valvular diseases than previously observed.

Although a bicuspid aortic valve was previously considered a relative contraindication for TAVR secondary to calcification and commissural abnormalities, leading to inadequate TAVR positioning and paravalvular leak, TAVR has now been successfully performed in a number of patients with bicuspid aortic valves.<sup>119,120</sup> Patients with bicuspid aortic valves were excluded from the initial SAPIEN and CoreValve trials, but subsequent registry data suggests similar mortality and PVL rates for TAVR in bicuspid and tricuspid valves.<sup>120,121 122 121</sup> Technological advancements with the newer Sapien 3, Evolut PRO, and Lotus valves (Boston Scientific Corporation; Natick, MA) promise to reduce PVL rates even further.

TAVR has also rarely been considered for pure AR, for which SAVR remains the preferred treatment due to a concern of an insufficient landing zone for TAVR with a non-calcified valve. Although new technologies are being developed for this indication, preliminary results indicate a lower successful implantation rate and higher rates of AR and mortality for pure AR TAVR.<sup>123,124</sup>

The role of valve-in-valve (VIV) procedures in treating bioprosthesis failure is becoming more prominent. Bioprosthetic valves are expected to have a durability of 10 to 20 years, such that patients who recently received bioprosthetic valves are being re-evaluated for surgery due to valve dysfunction. Aortic and mitral structural bioprosthetic valve deterioration that requires re-operation occurs in 20-30% of patients 10 years after initial SAVR, and in over 50% of patients after 15 years.<sup>125,126</sup> The primary reasons for bioprosthetic valve dysfunction are tissue deterioration secondary to cusp calcification and collagen deterioration.<sup>127</sup> Such patients are inevitably at higher re-operative risk, providing an opportunity for TAVR to pose an alternative to re-operative SAVR.<sup>128,129</sup> These patients have traditionally been managed with re-operative SAVR, with mortality rates ranging from 3% to 23%.<sup>130,131</sup>

Since the first case reports of VIV were published in 2007, both the Edwards and CoreValve systems have been most commonly used for aortic VIV.<sup>126,132</sup> Systematic reviews have demonstrated significant gradient improvements (59.2 to 23.2 mmHg mean gradient improvement) with VIV, comparable to SAVR, although with higher rates of PVL (3.3% vs 0.4%) and lower rates of stroke and bleeding

compared to re-op SAVR (1.9% vs 8.8% and 6.9% vs. 9.1%, respectively).<sup>133</sup> Rates of coronary obstruction (2.2%), valve malpositioning (12.4%), and elevated gradients (32.1% PPM rate) are higher for VIV than native valve TAVR, but permanent pacemaker implantation rates are lower.<sup>126</sup> These findings must be considered in light of the fact that VIV is typically performed in older patients with more severe comorbidities and higher operative risk. Challenges with VIV continue to be proper valve sizing to prevent placement of a too small valve that causes patient-prosthesis mismatch,<sup>126</sup> avoiding coronary obstruction,<sup>45</sup> and valve positioning.<sup>134</sup> There is less evidence with VIV TAVR-in-TAVR, but it is emerging as a viable option for TAVR dysfunction.<sup>135-137</sup> For mitral VIV and VIR procedures, the most commonly used valves have been the SAPIEN XT and MELODY valves, with acceptable hemodynamic and clinical results, but with high rates of residual regurgitation and LVOT obstruction.<sup>126</sup> At our institution, the rapid evolution of TAVR is already shaping SAVR decisions—bioprosthetic valve implantation is being considered for patients who otherwise may receive mechanical valves (for which VIV is not possible) with the expectation that TAVR technology will advance sufficiently over the next decade to avoid open-reoperation in these patients. Nonetheless, more data on long-term durability of VIV valves needs to be obtained to guide further clinical decisions.

## Cost-Effectiveness

As healthcare costs continue to rise, clinicians must become conscientious stewards of scarce healthcare resources and consider how they can deliver the most valuable care to patients. One tool to help clinicians evaluate resource allocation is cost-effectiveness—a metric of clinical benefit divided by the cost of an intervention. Reynolds et al. used the PARTNER Cohort B data to demonstrate the cost-effectiveness of TAVR compared to medical management among inoperable patients—although TAVR increased cumulative 1-year healthcare costs (\$106,076 vs. \$53,621), driven primarily by the index procedure and initial hospitalization, it drove down subsequent follow-up costs relative to medical management, and was calculated to have a cost-effectiveness ratio of \$50,200 per quality-adjusted life year (QALY) gained.<sup>138</sup> Multiple studies have also demonstrated the cost-effectiveness of TAVR relative to SAVR. Using PARTNER Cohort A data of high-risk patients with severe AS, Reynolds et al. demonstrated both lower 12-month costs and higher quality (as evaluated by Quality Adjusted Life Years [QALYs]) for transfemoral TAVR (tf-TAVR) compared to SAVR, making tf-TAVR economically dominant compared to SAVR.<sup>139</sup> The opposite was true of transapical TAVR (ta-TAVR).<sup>139</sup> For the CoreValve U.S. High Risk Pivotal Trial, Reynolds et al. demonstrated that while TAVR was more expensive than SAVR (\$11,260 higher for index admission, \$17,849 higher for lifetime cost), it was associated with a slight QALY benefit, resulting in a cost-effectiveness ratio

of \$55,090 per QALY gained.<sup>140</sup> With a slight reduction in CoreValve expense, the CoreValve TAVR system would fall within the standard academic cost-effective range of <\$50,000 per QALY gained.<sup>140</sup>

Cost-effectiveness analysis of the MitraClip using EVEREST II data depend on the pricing, which varies between the U.S. and Europe. Using the study price of \$18,000, MitraClip reduced costs per patient by \$2200, but the clinical outcomes of the MitraClip were so variable that conclusive cost-effectiveness recommendations could not be made.<sup>141</sup>

In addition to technologies, operative processes and systems should also be under scrutiny for effectiveness and value. Babaliaros et al. demonstrated that tf-TAVR performed in a cath lab (minimalist approach), compared to tf-TAVR performed in a hybrid operating room (standard approach), significantly lowered costs while preserving minimal morbidity and mortality and maintaining equivalent effectiveness.<sup>142</sup> The lower costs were secondary to shorter lengths of stay and less resource utilization.

As other transcatheter therapies become more mature, they should also be evaluated through the lens of cost-effectiveness in order to fully assess their benefit relative to conventional SAVR. Such studies should also be replicated for different patient risks groups as the data become available. Inevitably, cost-effectiveness calculations will change as the procedures become more widely available and less expensive, but such studies can help drive clinicians to consider how they can lower healthcare costs while maintaining the best clinical outcomes.

## **Interdisciplinary Approach—The Heart Valve Team**

As healthcare system debates persist at the forefront of national attention, clinicians should not only consider costs and resource allocation, but also systems issues around improved efficiency, teamwork, and decision-making.

Cardiac surgeons and interventional cardiologists stand at the forefront of these strategic innovations with the development of Heart Valve Teams to pre-operatively evaluate transcatheter valve candidates. As evidenced throughout this chapter, there is still much controversy around indications for TAVR vs. SAVR, which patients would make the best candidates for each type of procedure, and which type of valve to use. Furthermore, the lack of long-term outcomes data further complicates the discussion. Heart Valve Teams work to overcome this uncertainty through a shared-decision making model that involves cardiologists with structural valve expertise, cardiac surgeons, anesthesiologists, echocardiographers, radiologists, valve coordinators, nurses, and others. The team brings together each member's experience and expertise to evaluate the risks and benefits associated with different treatment options for each patient. Heart Valve Team members should be encouraged to share this interdisciplinary collaborative practice with their colleagues in other specialties, in order to foster shared-decision making throughout healthcare.

## Conclusion

Since the turn of the century, the field of cardiac surgery has been disrupted by novel transcatheter technologies that promise to upend traditional open management strategies for patients with valvular disease. Just like any disruptive technology, as was seen with PCI in the 1970s and 1980s, initially seemingly inferior technologies that have risk profiles acceptable only to high-surgical-risk patients eventually become perfected to offer superior solutions to a wide variety of patients, supplanting the status quo. Although still in their early stages, transcatheter therapies offer hope for previously inoperable patients and, with continues improvements, promise to provide alternatives even for previously intermediate- or low-risk patients.

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## **PROJECT 3: EVALUATION OF ACCOUNTABLE CARE ORGANIZATIONS**

### **Hospital-based Accountable Care Organization Success May be Limited by Ability to Track Performance Indicators**

#### **Abstract**

Accountable care organizations (ACOs) have emerged as one of the leading proposals to reduce costs, improve quality, and shift the United States healthcare system from volume-based care to value-based care. Because ACOs haven't achieved the degree of cost reductions and quality improvements initially hoped for, we sought to better understand the underlying reasons for their limited success. We investigated hospital-based ACOs' abilities to track and share performance and financial metrics, using data from the AHA's 2015 Survey of Care Systems and Payment. We found that few ACOs have the capability to track and share performance metrics (especially financial metrics), and those that do are more likely to have taken on more financial risk. Our findings highlight the challenges implementing value-based healthcare through the ACO model, a broad-stroke tool, and suggest a sharper tool, like bundled payments, may be more successful.

#### **Introduction:**

Accountable care organizations (ACOs) and bundled payments have emerged as the leading proposals to help reduce costs, improve quality and shift the United States healthcare system from volume-based care to value-based care. ACOs are groups of health care providers working together to provide coordinated care for their patients, with the goal of improving quality while avoiding unnecessary services. (1) ACOs share in cost savings achieved from improved coordination. The number of ACOs in the US is growing: there were 923 ACOs covering more than 32 million lives at the end of Q1 2017, an 11% growth from 2016. (2)

Despite their promise, ACOs have had mixed success. (3) ACOs haven't achieved the degree of cost reductions and quality improvements initially hoped for, with analyses showing 1-2% annual per beneficiary savings that are largely undone by bonus payments for program participation. (4, 5) Although several groups have studied ACOs' progress, there is little published data on whether ACOs have the necessary internal capabilities to track cost and quality metrics. (6) (7) Early data suggest that ACOs have limited financial and quality monitoring tools, and may lack key capabilities in IT infrastructure and care management processes. (6)

We sought to better understand the underlying reasons for the limited success of hospital-based ACOs by investigating their ability to track and share performance and financial metrics. We found that few ACOs have these capabilities (see Exhibit 2 and 3), and those that do are more likely to have taken on higher levels of financial risk (see Exhibit 6).

### **Study Data and Methods:**

We used data from the American Hospital Association's 2015 Survey of Care Systems and Payment, which tracks the evolution of new care delivery and payment models among hospitals. The survey was sent to all hospitals in the United States in January 2016, and data were collected from January to April 2016. Survey questions are available in the Supplemental Material. Our analysis included only general medical and surgical hospitals (n=535). The response rate for this group was 42%.

### **Study Results:**

#### ***Hospital-based ACOs are evenly distributed across all hospital types***

Hospitals of all sizes and types have developed ACOs (Exhibit 1). Not-for-profit hospitals – including academic medical centers – are the most common type of hospital to develop ACOs. The distribution of the type of hospitals that has developed ACOs was relatively consistent across hospitals of different sizes.

#### ***Most Hospital-based ACOs do not track and share performance metrics***

Fifty-two percent of respondents measure cost and efficiency indicators, while 64% and 84% track patient satisfaction and clinical quality indicators, respectively (Exhibit 2). Hospital-based ACOs indicate that they plan to increase their collection of these metrics in the future (Exhibit 2). A smaller portion – 52% of ACOs – both track and *share* these metrics with all providers in the ACO. Of those that track and share metrics, 84% are measuring clinical quality indicators, 63% are tracking financial metrics, 76% are tracking utilization metrics (the services their patients are using and how often) and 57% are measuring patient satisfaction (Exhibit 3).

#### ***Not all ACOs can track patient level services and costs***

As an ACO, a provider organization takes on financial risk by committing to spend a certain amount of money on a specified patient population per year; however, only 41% of hospital-based ACOs are able to verify patient eligibility and benefits. Fifty-nine percent have information systems to track utilization of services and 31% have a “process to conduct ongoing monitoring of services rendered and the cost for those services compared to the revenue received” (Exhibit 4). This is surprising given that our analysis is limited to hospital-based ACOs, which we expect to be better equipped to track this type of data. By 2015, 96% of hospitals had a certified EHR and 84% had fully adopted their EHR. EHRs track every patient encounter, so hospitals should be able to leverage their EHRs to at least track utilization of services within their system. (8) Patients will also use services outside of the hospital system, in which case hospitals would have to rely on data from payers (i.e., claims data) in order to track their patients’ utilization.

***ACOs that take on more risk are more likely to have better financial data-tracking capabilities***

ACOs are typically in one of four financial risk models, all of which are predicated on a pre-arranged target amount for the cost of caring for a group of patients for one calendar year:

- One-sided risk model: Providers receive a share of savings below the cost of care target, and do not share in the losses if the cost exceeds the target.
- Two-sided risk model: Providers receive the same share of savings below the target, but they pay a share of any costs that exceed the target.
- Global payment under fee-for-service model: Providers receive 100% of any savings they generate below the target, and are responsible for all costs that exceed the target.
- Partial capitation model: Providers receives a per-member, per-month (PMPM) fee for primary care and coordination, but other services (e.g. specialty care, procedures, or hospitalizations) are paid in a traditional fee-for-service model. If the annual cost of care is above the target, the ACO has to return all or a portion of the PMPM fees.

The majority of the hospital-based ACOs included in the AHA survey are in one-sided risk contracts (Exhibit 5). ACOs that take on a greater level of financial risk are more likely to track and share cost and efficiency indicators and to be able to track services rendered. For example, among ACOs in one-sided risk arrangements, 45% report that they are tracking cost and

efficiency indicators, compared to 63% of those in a two-sided risk model, and 79% of those in a global payment model (the highest level of financial risk) (Exhibit 6). The same pattern is true for the ability to track services rendered: 28% had this capability of those in one-sided risk contracts compared to 37% in two-sided and 57% in global payment contracts (Exhibit 6).

### **Discussion:**

Although ACOs were created as a way to change the delivery of healthcare by incentivizing coordinated care, our results highlight several areas of concern.

#### ***Most Hospital-based ACOs do not track and share performance metrics***

Only 32% of hospital-based ACOs are tracking and sharing financial metrics with their providers. It is unclear how providers can know if they are indeed providing higher-value care if they are not aware of the financial implications of the care their patients receive. Previous studies have shown that when providers are aware of the costs associated with the care they are providing in real time, they choose less costly options. (9)

#### ***Not all ACOs can track patient level services and costs***

An additional issue facing hospital-based ACOs is that depending on how patients are attributed to ACOs, organizations and physicians do not know until the end of a calendar year which patients are in the ACO. (10) Given this issue of patient attribution and the finding that 69% of ACOs cannot track patient utilization of services and charges for those services in real-time, it is unclear how these ACOs can make changes to improve care coordination and avoid unnecessary services.

#### ***ACOs track facility-level data***

ACOs that track clinical quality, patient satisfaction, and financial data track this data at the level of the facility rather than at the level of a department or individual provider. In order to know what changes to make in their prescribing and referral patterns, physicians need individual-level performance metrics and data. Facility-level data does not give providers actionable information: first, it is not clear which providers are performing well and which need to improve; and second,

it allows for a diffusion of responsibility across the system rather than requiring providers or departments to take responsibility for their performance. (11)

### ***ACOs that take on more risk are more likely to have better financial data-tracking capabilities***

Given our findings that suggest that many hospital-based ACOs do not have adequate tools to track and manage cost and quality, it is not surprising that those ACOs that have taken on more risk are likely better-equipped to manage patient-level costs and decisions that impact those costs, such as referral patterns, and their ability to manage these variables likely impacted their decision to take on more financial risk.

### ***Are ACOs the right approach?***

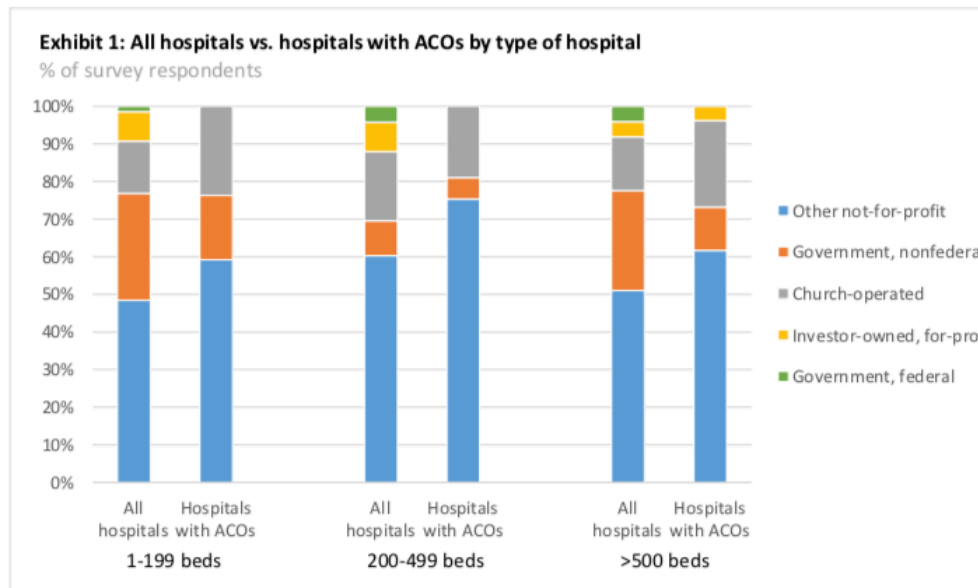
It may be easier for hospital systems to implement other types of value-based care such as bundled payments, which focus on an episode of care rather than the patient as the fundamental cost-accounting unit. Given that there will be fewer care variations in a typical bundle than an average ACO, care utilization and finances will likely be easier to track, at least within the walls of the hospital itself. Bundled payments are less daunting for institutions to adopt: hospitals can decide to contract for bundled payments only in departments where they are already high performing. Then they can learn how to succeed with a bundled payment in one department and pass on best practices to others.

## **Conclusion**

The ACO is a broad-stroke model for changing how healthcare is delivered. This analysis highlights why a broad tool is challenging: it is difficult to get data at the level of granularity required to resonate with individuals, and physicians have limited control over the wide range of care their patients receive over the course of a year. A sharper tool, like bundled payments, where one defined episode of care, can be studied, measured, and perfected, may be a better answer.

**Exhibit 1: All hospitals vs. hospitals with ACOs by type of hospital**  
% of respondents

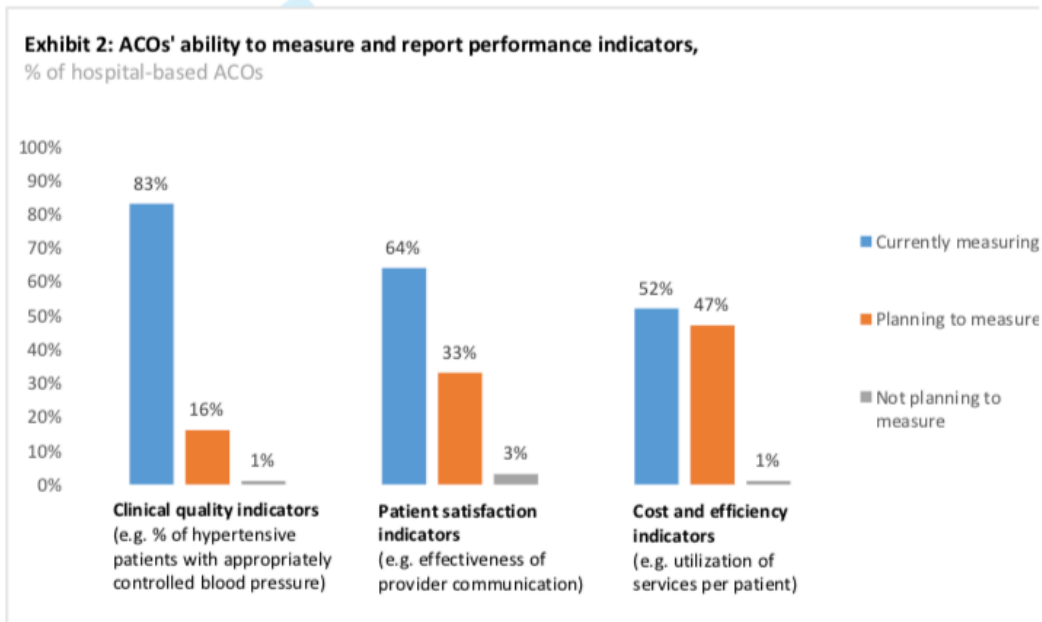
Bed Size	1 to 199		200-499		>500	
	All hospitals	Hospitals with ACOs	All hospitals	Hospitals with ACOs	All hospitals	Hospitals with ACOs
Other not-for-profit	48%	59%	60%	75%	51%	62%
Government, nonfederal	28%	17%	9%	6%	27%	12%
Church-operated	14%	24%	18%	19%	14%	23%
Investor-owned, for-profit	8%	0%	8%	0%	4%	4%
Government, federal	1%	0%	4%	0%	4%	0%



## Exhibit 2: ACOs' ability to measure and report performance indicators

% of hospital-based ACOs

	Clinical quality indicators	Patient satisfaction indicators	Cost and efficiency indicators
Currently measuring	83%	64%	52%
Planning to measure	16%	33%	47%
Not planning to measure	1%	3%	1%



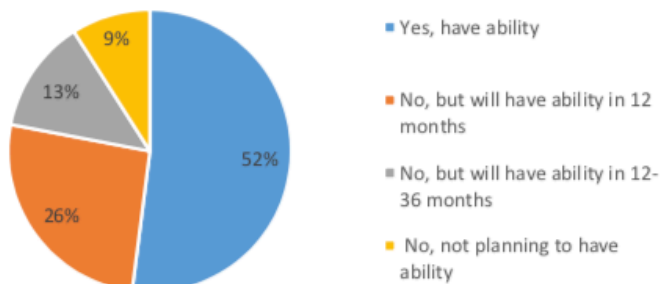
**Exhibit 3a: ACOs' ability to track and share performance measures with all**  
% of hospital-based ACOs

Yes, have ability	52%
No, but will have ability in 12 months	26%
No, but will have ability in 12-36 months	13%
No, not planning to have ability	9%

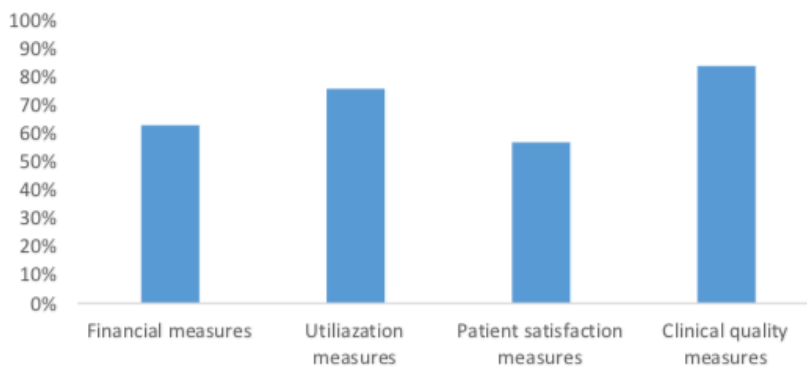
**Exhibit 3b: Types of performance measures tracked**  
% of "YES" respondents

Financial measures	63%
Utilization measures	76%
Patient satisfaction measures	57%
Clinical quality measures	84%

**Exhibit 3a: ACOs' ability to track and share performance measures with all providers in ACO**  
% of hospital-based ACOs



**Exhibit 3b: Type of performance measures tracked**  
% of "yes" respondents

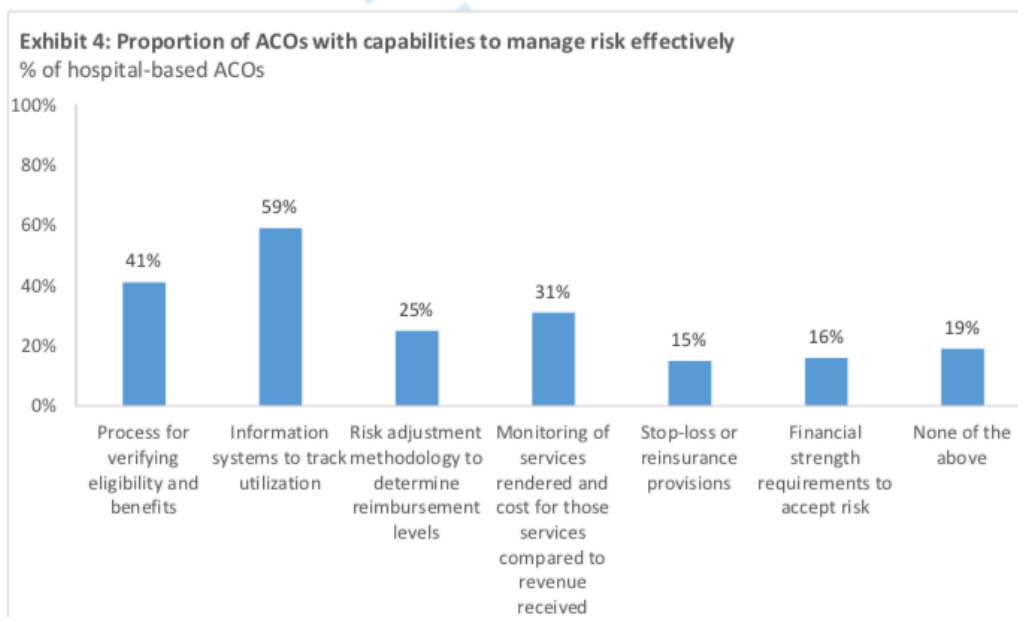




#### Exhibit 4: Proportion of ACOs with capabilities to manage risk effectively

% of hospital-based ACOs

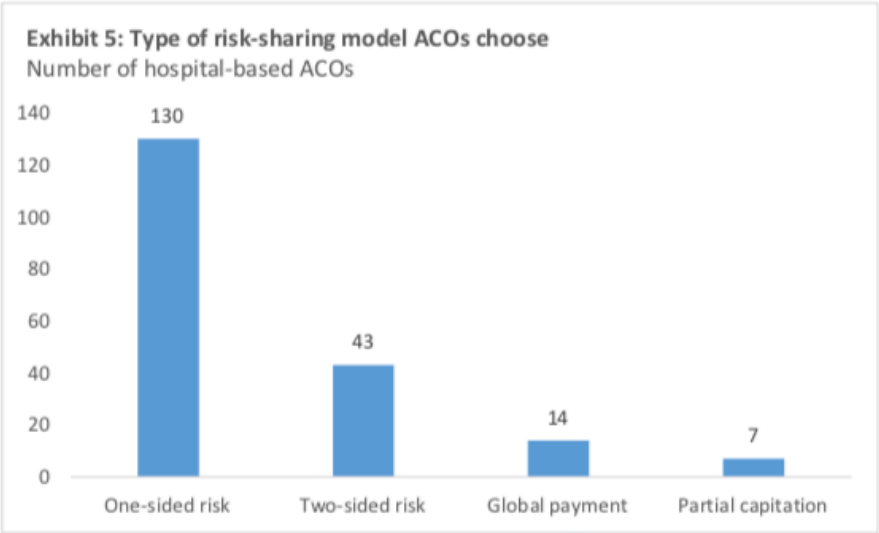
Process for verifying eligibility and benefits	41%
Information systems to track utilization	59%
Risk adjustment methodology to determine reimbursement levels	25%
Monitoring of services rendered and cost for those services compared to revenue received	31%
Stop-loss or reinsurance provisions	15%
Financial strength requirements to accept risk	16%
None of the above	19%



**Exhibit 5: Risk-sharing models ACOs choose**

Number of hospital-based ACOs

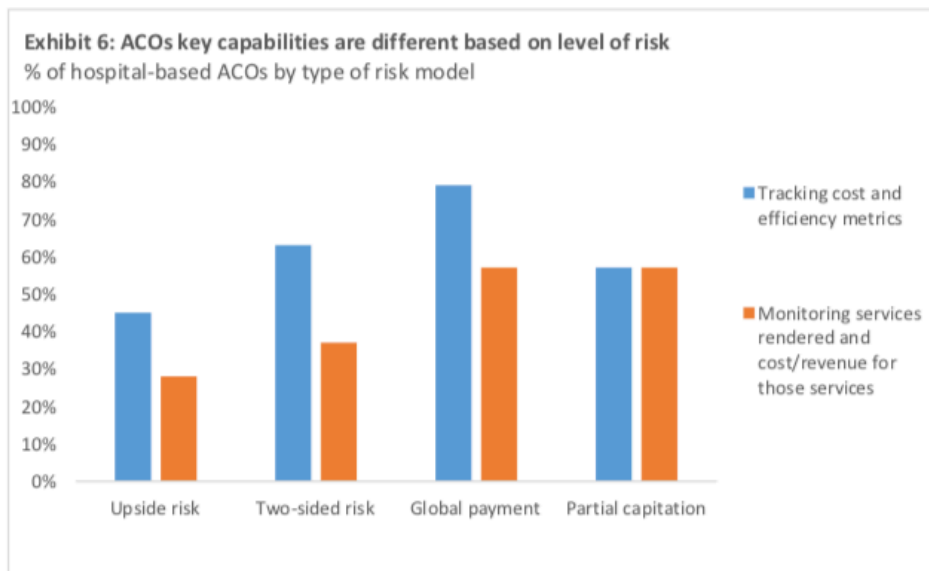
One-sided risk	130
Two-sided risk	43
Global payment	14
Partial capitation	7
	<b>194</b>



# Exhibit 6: ACOs' key capabilities are different based on level of risk

% of hospital-based ACOs by type of risk model

	Tracking cost and efficiency metrics	Monitoring services rendered and cost/revenue for those services
Upside risk	45%	28%
Two-sided risk	63%	37%
Global payment	79%	57%
Partial capitation	57%	57%



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