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## Introduction

In most countries the cost of health care has progressively increased at a rate greater than the respective national economic growth [1]. Consequently, health-care delivery in its present state is unsustainable and in many countries has already resulted in increased taxation as well as decreased government funding of other vital societal services. From a macroeconomic perspective the economic impact of health-care interventions is critically important to all stakeholders. As stakeholders in health-care management and delivery attempt to mitigate increasing expenditures, greater demands are made upon all therapies to describe their proven indications, report adverse events, and delineate their outcomes [2].

With increasing costs, it also becomes necessary for health providers and payers to assess the value (defined as the relative worth, utility, or importance) of an intervention compared to alternative interventions. These needs have been highlighted by the Institute of Medicine (IOM) as comparative effectiveness research (CER). As per the IOM “*Comparative effectiveness research is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels*” [3–5]. Physicians have traditionally understood and taken the perspective of safety and clinical efficacy of an intervention. However, physicians often lack the perspective

and language of purchasers and policy makers, which also includes the health economic aspect of not only the intervention of interest to a specific health provider, but also its impact and relevance to other relevant interventions and health-care delivery as a whole.

## Health Economic Evaluations (HEEs)

### The Importance of Health Economic Evaluations

From the perspective of musculoskeletal surgery, the increasing demands for surgical services will only continue to increase [6–13]. It is estimated that by the year 2030, over half of the adults in the US population will be aged over 65 years. The economic effects of degenerative disorders such as arthritis of the spine (i.e., spinal stenosis), hip, and knee within this aging population will have profound implications on the future affordability and availability of quality spine care [6–13]. Within spine surgery, the SPORT studies [14–17] have documented the sustainable efficacy and cost-effectiveness of interventions using traditional open surgery techniques for lumbar disk herniation, spinal stenosis, and degenerative spondylolisthesis compared to nonsurgical care at the 4-year mark. However, CER within the spine surgery literature from an economic perspective is generally lacking and requires further research. Although the need for economic data in the current health-care climate is increasingly important, less than 1 % of articles published on lumbar spine fusion between 2004 and 2009 include a cost-effectiveness analysis (CEA) [18]. In addition, societal perceptions regarding spine surgery and its benefits, risk, and associated costs may also have an impact on the perceived value of spinal intervention, regardless of whether it demonstrates cost-effectiveness or not. Unfortunately, as a result of heterogeneity of spine surgery, particularly around the surgical management of low back pain, spine surgical interventions are perceived to be high risk, high cost, often

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ineffective, and often seen as a last resort. In addition, the high variability in results along with differences in clinical indications and techniques used further confounds existing opinions regarding spine surgery and surgical techniques [8]. Furthermore, from the non-spine surgeon perspective, much of what is done in spine surgery (good and bad) is lumped into one seemingly homogenous category that typically equates to the management of low back pain.

With these aforementioned challenges in mind, it is critically important for a spine surgeon to understand that the value of spine intervention for degenerative conditions must also be looked at from a big-picture perspective (i.e., societal and payer perspective). As health-care resources contract, resource allocation for competing pathologies including cancer and chronic conditions such as cardiovascular disorders, diabetes, cancer, and arthritis currently demands the largest portion of available funds. In a paper by Martin et al. that looked at expenditures and health status among US adults with back and neck problems, the authors noted significantly escalating cost with no appreciable improvement in health status compared to non-back/neck individuals [19]. Furthermore, the estimated annual US expenditures for back and neck problems (\$86 billion) have reached levels comparable to diabetes (\$98 billion), cancer (\$89 billion), and non-spine arthritis (\$80 billion). These are all second to heart and stroke expenditures which are estimated at \$260 billion. A discussion of societal and payer prioritization regarding relative health-care resource allocation is clearly a complex issue which is not within the scope of this chapter, but is worthy of mention to enable the reader to keep the broader perspective of payers and policy makers in mind as they increase their personal understanding of CER.

## The Language of Health Economic Analysis

A detailed description of HEE is not within the scope of this text and thus only fundamental concepts relevant to a surgeon, from the perspective of a clinician/surgeon will be provided [20]. A common misconception from physicians and surgeons is that all HEEs are the same (as many health economists may erroneously perceive all spine surgery to be the same) and only consider the bottom line (i.e., cost). The reality is that there are several types of HEE that are not interchangeable and require a better understanding when a clinician is considering the merit of an HEE. Some HEEs only consider cost and make the assumption that the clinical efficacy is equal between the intervention of interest, whereas others consider both the relative cost and efficacy of the intervention. Furthermore, it is critical to understand the perspective of the costing data source(s) and whether it only considers some or all health-care cost (direct and/or indirect[e.g., overhead]) attributable to a specific intervention and whether societal cost, such as productivity, has been included [20, 21]. Another important aspect of an

HEE is the time horizon in which the analysis has been considered (e.g., perioperative period only or estimated over the lifetime of the patient) and whether the assumptions and variability associated with critical analytic parameters are accurate and accounted for. For HEEs where the outcome effects and cost are estimated for the lifetime of the patient, future costs and utilities are typically discounted to adjust for society's relative value placed on immediate costs and benefits compared to those in the future, a concept known as time preference [21]. Commonly, resources in the present are preferred over future resources since benefit can be derived from present resources in the interim. Most importantly when comparing interventions within the same analysis or across different analyses, it is critical to ensure that compatible clinical, costing, analytic model assumptions and overall economic analysis and perspective were employed between groups. Variations in these critical parameters can profoundly impact the outcome and interpretation of an HEE. Consequently, an important part of an HEE is the inclusion sensitivity analysis within the methodology. This enables relevant and realistic variation of important clinical and economic parameters to assess the robustness of the HEE findings and allows the reader to interpret the results based on alternate parameters that may be more consistent with their local health-care system [21].

As HEEs can be accomplished in a number of ways and customized to specific objectives, the outcome will be potentially interpreted differently based on the perspective taken by different stakeholders (i.e., value is in the eye of the beholder). For example, from the perspective of a private payer, the primary goal might be to obtain the greatest return on their investment. From a physician's perspective, patient outcomes and clinical outcomes such as procedural time or adverse events, regardless of the economic aspect, might be the major issues of consideration. From the patient's or a societal viewpoint, personal factors such as quality of life post-surgery, recovery time, and ongoing costs along with activity factors such as days of work missed and productivity losses may be most relevant.

## Definitions of HEEs

The most basic type of economic analysis is cost analysis (CA) which compares the cost of health-care interventions and does not consider differences in health outcomes [20]. This type of analysis is obviously very "payer" focused; it evaluates interventions based on their costs only, and from a clinical perspective this type of analysis is not useful for CER, but represents the most common analysis in the spine surgical literature. Another type of economic analysis is cost-minimization analysis (CMA) which determines and evaluates the least expensive interventions among the interventions that have demonstrated the same outcomes. This type of analysis may be tedious to complete because

one must truly demonstrate that the resulting outcomes between interventions are in fact the same, quite a feat for health-care issues which are often multifactorial and dynamic. A CMA can be effective at any level where reducing expenditure is a priority and therapeutic equipoise from high-quality evidence has been established between two interventions for the same diagnostic/clinical scenario. A cost-benefit analysis (CBA) refers to an HEE where both the cost of the interventions and their outcome are assessed in terms of dollars. It is reflected as the ratio of the difference in outcome (e.g., cost difference of length of stay between two interventions) over the difference in cost. A CBA ratio greater than 1 suggests a cost-benefit of the intervention under evaluation. From a CER perspective, a cost-effectiveness analysis (CEA) which simultaneously considers both the comparative clinical effectiveness and cost of intervention is the HEE method of choice [20]. Thus, being cost-effective does not necessarily mean an intervention is less expensive up front.

### Cost-Effectiveness (CEA) and Utility (CUA) Analyses

The primary premise of a CEA is the measurement of the incremental cost and effects that result from choosing one intervention option over another [22, 23]. The purpose is to assist key decision makers in determining how to allocate resources across a defined number of competing needs to optimize health outcomes, while adhering to budgetary constraints [23]. CEA is distinct from the aforementioned economic analyses such as a CA or CBA, as it simultaneously consider clinical effectiveness and cost. Within health care, CEA is utilized in scenarios where assigning a monetary value on a health effect might be inappropriate. A CEA is typically calculated using an incremental cost-effectiveness ratio (ICER), which equals the cost of a new strategy less the cost of current practice, divided by the clinical change in outcome of the new strategy, minus the current practice [24].

$$\text{ICER} = \frac{\text{Cost}_{\text{new strategy}} - \text{Cost}_{\text{current practice}}}{\text{Effect}_{\text{new strategy}} - \text{Effect}_{\text{current practice}}}$$

The ICER analysis typically makes the assumption that the new strategy is likely to cost more but has a clinically greater effect and is hence used to determine the cost per incremental difference in outcome.

### Components of a CEA

As stated previously, economic analysis can be a very complex task, especially when cause and effect relationships are not very easily discerned. Another aspect which increases difficulty is the sheer volume of variables that can contribute

to the overall costs of a health intervention. Often, it can be beneficial to break down the analysis into two smaller analyses: factors that directly contribute to cost against factors which indirectly affect it.

### Direct Costs

Direct costs are tangible costs such as the cost of medical tests, implants, operating room time, rehabilitation, or out of pocket cost for payment of services that an individual may no longer be able to perform as a direct result of a disease state.

Proponents [25–31] of minimally invasive procedures frequently cite the advantage of MIS versus open surgery is its ability to lower postoperative morbidity. In a recent review, Allen and Garfin outline the factors in open procedures that may increase cost relative to MIS [32]. Factors such as increased blood loss (and transfusion rates), extended OR time, and the use of open posterior approach to the spine significantly increase the likelihood of an infection and other related morbidity (e.g., pain) and adverse events [32–34]. For example, the costs surrounding a unit of blood transfused are estimated to be just under \$1,200, and this measure is often associated with increased LOS and resource utilization [32]. Kalanithi et al. reported that each in-hospital complication for spine patients was associated with an increased cost of 10,000 USD and rising to over three times the cost of procedure if any readmission and revision surgeries were performed [33]. Khan et al. reported that a single complication may increase hospital costs for a patient in general surgery (except cardiac) by up to 79 % [35]. Broken down further, the median costs per complication resulted in costs of 4,278 USD (range, 2,511–25,168 USD) and as a result increased LOS by 11–297 % [35]. When complications occur, significant increases in LOS, mean total charges, and in-hospital mortality are observed [33]. Consequently, taking steps to decrease the probability of adverse events and reduce LOS by using MIS techniques as well as other available interventions may help lower these associated costs substantially.

### Indirect Costs

By definition these costs are more subjective and consequently much more variable depending on what is considered to be indirectly associated with a given disease state or intervention. Consequently, the determination of indirect cost is typically much more difficult. In their simplest form, indirect cost can be those associated with direct medical cost (e.g., the estimated institutional overhead to provide a particular service). More commonly, indirect costs refer to societal cost such as lost productivity. However, it is also important to consider that many indirect costs from a societal perspective may also be very closely related to direct costs,

further increasing complexity. For example, postoperative complications such as infections following surgery may result in longer hospital stays, greater recovery time, and additional medication costs contributing to an overall decline in health. These direct costs also have an effect on societal indirect costs as the individual may be out of the work force for a longer time, thereby decreasing their productivity. Thus, isolating and analyzing costs independently of each other can be very difficult, and results must be interpreted within a defined context and in relation to other factors as opposed to individually.

From a macroeconomic perspective, the societal costs of low back pain can be substantial. LBP has become the second most common reason for patients to visit primary care providers [36]. A recent systematic review of studies on the cost of low back pain noted that costs resulting from lost productivity and early retirement were the largest component of total costs, representing a median of 85 % of overall costs [37]. Consequently, indirect cost, particularly from a societal perspective, is an important measure of postoperative ongoing cost beyond discharge from hospital and provides a more comprehensive allocation of the costs associated with any intervention. In a 2004 study, Fritzell et al. reported that treating an individual with open lumbar fusion surgery was less expensive (and thus more beneficial) than to have the person not contribute to societal productivity while receiving conservative care treatment [38, 39]. In theory, those indirect benefits would increase if the surgical intervention resulted in less morbidity, faster recovery, and resumption of functional activity (e.g., work); in other words the promise of MIS should result in reduced cost.

## Effectiveness

Effectiveness can be measured in a variety of ways depending on the most relevant outcome of the interventions assessed. For example, if mortality rate was the best outcome measure for a new therapy, the cost-effectiveness could be represented as the incremental cost per additional life saved or cost per adverse event avoided if the outcome of interest is morbidity. For elective surgical procedures the most common form of a CEA is a cost-utility analysis (CUA), which measures effectiveness using a generic health utility score that allows the comparison of different health outcomes by measuring them all in terms of a single unit—the quality-adjusted life-year (QALY). A QALY is a generic measure of the burden of a disease on life and encompasses both the quality and quantity of life lived [18, 21]. Thus, for HEEs it represents both the effect size and durability of a given intervention.

A QALY is an index number that is calculated by multiplying the utility score of that treatment by the duration of

treatment effect. The utility score represents the health-related quality-of-life value in a range from 0 to 1, with 0 representing death and 1 representing the best or perfect health state. The utility score used to calculate the QALY of an intervention has been derived from several existing generic health-related measures, including the EQ-5D, Health Utilities Index, Quality of Well-Being Scale, and SF-36 (expressed as SF-6D) [40–48]. Consequently, the QALY is an outcome measure that enables decision makers to compare the effectiveness of interventions across many different areas of medicine and disease states. For this purpose decision makers utilize CEAs (and specifically CUAs) to identify the costs associated in achieving a single QALY (i.e., the relative value of a given intervention). It is important to note that currently available health utility scores are not interchangeable as they often generate different values from within the same population, and thus the cost/QALY values may differ depending on which utility score was utilized [40, 47, 48].

Equally important to the QALY effect size of an intervention on the health utility determination of an individual or population is the ability of an intervention to maintain that improved health state (i.e., the durability of the treatment effect) [14, 18, 21]. Tosteson et al. have recently demonstrated this concept in the spine literature [14]. In their report of the 4-year cost-effectiveness of surgery versus nonoperative treatment from the SPORT studies, the authors demonstrated sustainable superior results (QALYs gained) from surgical compared to nonsurgical treatment. This corresponded to an improvement in the cost/QALY ratio (ICUR) at 4 years compared to 2 years for all three subpopulations studied. For spinal stenosis, the 2- and 4-year ICUR for surgery compared to nonoperative treatment was \$77,600 and 59,400. For the treatment of intervertebral disk herniation, the ICUR decreased from \$34,355 at 2 years to \$20,600 at 4 years. The greatest improvement was seen for the degenerative spondylolisthesis cohort, where the ICUR went down to \$64,300 at 4 years compared to \$115,600 at 2 years. In more traditional economic models, where the QALY is estimated over the lifetime of the patient based on reference case data, the ICUR will typically reduce below \$10,000/QALY for musculoskeletal interventions such as hip and knee replacement or 1–2-level spinal stenosis surgery [49].

Finally, when faced with a cost per QALY evaluation, recommendations exist regarding the threshold for which an intervention is considered cost-effective. Generally, an ICUR greater than \$100,000 per QALY is considered too costly for the utility gained [50, 51]. This number can vary from country to country and typically ranges 50–100 K USD/QALY [21]. Furthermore, the number may vary depending on the clinical context that is being considered based on the local societal value of the given intervention (e.g., life-extending cancer surgery vs. improvement on quality of life).

**Table 3.1** Principle approach to determining the need for a formal cost-effectiveness analysis (CEA)

Effectiveness of new strategy	Costs of new strategy	
	Costs more	Costs less
More effective	CEA relevant	<b>New strategy is dominant—adopt</b>
Less effective	<b>New strategy is ineffective—abandon</b>	CEA relevant

### Clinician's Approach to HEE for MIS of the Spine

Table 3.1 demonstrates the possible relationships between cost and effectiveness and can be utilized to better discern when a CEA might be worthwhile [20]. Simply put, if a new intervention provides better outcomes and reduced cost, it has greater value than the current treatment and should be adopted. Conversely, if a new procedure is less effective and cost more, it should not be supported in its current form. All other scenarios typically will require a formal CEA to determine the relative value of an intervention compared to its alternatives [20]. From this fundamental approach, the first step would be the need to answer the question of whether or not MIS of the spine is clinically more or less effective compared to open surgery.

In the last 2 years, an increasing number of cohort studies comparing open versus MIS posterior lumbar fusion techniques for degenerative conditions have been published. Details of outcomes for specific techniques are available in chapters specific to certain MIS techniques. We are currently in the process of a systematic review assessing the comparative effectiveness of MIS versus open posterior fusion for degenerative lumbar conditions. To date, we included 16 English language publications meeting our inclusion criteria (same center comparative cohorts, with at least ten patients in each group and at least one of the following outcomes: patient-reported outcome measure(s), perioperative data (blood loss, surgical time, length of hospital stay), radiographic outcomes, complications, and economic evaluation) [25–31, 52–60]. Using the GRADE system, the quality of evidence was low (6) to very low (8) in the majority and moderate in two and high in only one paper [61]. As demonstrated in Table 3.2, the patient-reported clinical outcome at the specified time intervals suggests, at least qualitatively, comparable outcomes between the MIS and open cohorts at 1 and 2 or more years of follow-up. No study demonstrated an inferior patient-reported outcome with the MIS cohorts.

Additionally, our review also compared the specific perioperative outcomes of EBL, LOS, transfusion rate, and OR time. As demonstrated by others, the MIS cohorts performed significantly better than the open group in these aspects. In other literature reviews encompassing transforaminal and posterior lumbar interbody fusion (TLIF and PLIF) as well

as extreme and direct lateral interbody fusion (XLIF/DLIF) techniques, Karikari et al. and Youssef et al. have demonstrated results regarding perioperative outcomes favoring the MIS techniques compared to open cohorts or historical controls [62, 63]. Karikari et al. specifically demonstrated that in all studies reviewed ( $n=7$ ) the MIS subgroup performed significantly better than the open group in perioperative measures (e.g., EBL, LOS, and OR time) [62]. In a recent meta-analysis performed by Wu et al. (2010), the authors assessed the fusion rate of MIS versus open TLIFs [64]. Using 16 studies for open TLIF ( $n=716$  patients) and 8 MIS studies ( $n=312$  patients), they reported no difference in the fusion rate between open (90.9 %, 95 % CI; 86.4–94.0 %) and MIS TLIF (94.8 %, 95 % CI; 85.4–98.3 %). They also noted that the reported complication rates trended toward a lower rate in MIS (7.5 %, 95 % CI; 3.0–17.3 %) versus open (12.6 %, 95 % CI; 7.5–20.3 %) TLIF. The authors appropriately cautioned that there was significant variability in reporting and a lack of clear definition as to what constituted a complication. In another recent review, Parker et al. assessed the infection rate between MIS and open TLIF and reported a significantly reduced rate for MIS (0.6 %) versus open (4.0 %) TLIF [65].

Considering the current available literature, one could conservatively conclude that MIS fusion in the lumbar spine demonstrates superior perioperative quality and clinical process outcomes and comparable midterm (1–2 year) radiographic and patient-reported outcomes. However, from an economic perspective there are several up-front additional costs associated with MIS fusion such as increased operative time during the learning curve, implant and disposable costs, dependence on the use of intraoperative imaging and associated resources, education and training, and a possible higher reoperation rate required for the removal of prominent or symptomatic implants. In the context of CER, the next logical step is to examine the CEA of MIS versus open fusion. In other words, one must determine the incremental cost of the demonstrated short-term perioperative benefits of MIS fusions.

### Economic Comparison of MIS Versus Open Fusion

In an excellent review of this topic, Allen and Garfin note the increasing importance of CEA in our current health-care environment. However, the authors point out the general lack of HEEs in the currently available literature [18, 32]. In addition, the authors importantly note that a “consistent method of exactly which cost to include, and how to accurately measure direct and indirect cost is yet to be defined in spine care, and existing cost analyses of spine care vary widely in their methods of measurement” [32]. As noted previously in the

**Table 3.2** Summary of comparative literature presenting patient-reported outcomes for posterior MIS versus open lumbar fusion techniques

Study author Study origin	Principle diagnosis	Mean follow-up			
		6–12 weeks Outcome	6 months Outcome	1 year Outcome	2 year + Outcome
Park et al. [27] Korea	Mixed		MIS	MIS	
Scheufler et al. [28] Switzerland	Mixed	MIS	MIS	MIS	
Dhall et al. [60] USA	Mixed				Equivalent
Starkweather et al. [26] USA	Instability	MIS			
Kasis et al. [25] UK	Mixed				MIS
Tsutomimoto et al. [52] Japan	Degenerative spondylolisthesis	Equivalent		Equivalent	Equivalent
Peng et al. [53] Singapore	Mixed		Equivalent		Equivalent
Gahreman et al. [54] Australia	Isthmic or degenerative spondylolisthesis (<50 % slip)			Equivalent	
Ntoukas et al. [55] Germany	Mixed	MIS		Equivalent	
Wang et al. [56] China	Degenerative spondylolisthesis				Equivalent
Wang et al. [29] China	Mixed	MIS	MIS		MIS
Kotani et al. [30] Japan	Degenerative spondylolisthesis	MIS	MIS	MIS	MIS
Rampersaud et al. [31] Canada	Isthmic or degenerative spondylolisthesis (<50 % slip)			MIS	
Adogwa et al. [57] USA	Degenerative spondylolisthesis				Equivalent
Lee et al. [58] Singapore	Mixed		Equivalent		Equivalent
Mobbs et al. [59] Australia	Mixed			Equivalent	

Note: Mixed diagnoses refer to varying combinations of degenerative disk, stenosis, spondylolisthesis, and other instability

section covering HEE, when assessing a CEA the main drivers that need to be considered are the relative cost (direct cost of index procedure) as well as ongoing cost and indirect (e.g., productivity) and effect size and durability of the outcome gained.

In other surgical specialties, cost-effectiveness has been demonstrated comparing MIS and open surgical techniques. An excellent example is provided by Bijen et al. in a systematic review of the cost and effects of abdominal versus laparoscopic hysterectomy [66]. In this study the authors demonstrated that although the total procedural costs were greater for MIS intervention (6.1 % in this particular procedure), decreased length of hospital stay, fewer complications, and lower indirect cost compensated for the greater initial cost. Whether the perioperative benefits demonstrated for MIS fusion compensate for the aforementioned higher cost, associated MIS fusion is yet to be determined in any comprehensive manner. To date, no high-level prospective or randomized studies have included a CEA in the comparison

of MIS techniques to open surgery or nonsurgical treatment of spinal disorders. More recently, economic considerations have been included in a handful of MIS versus open fusion retrospective cohort studies [29, 31, 56, 65, 67]; however, as noted in our current systematic review, the quality of evidence is generally low and the economic perspective and methodology of these studies are varied. If, as suggested by the current comparative literature, MIS fusion does in fact consistently provide significant short-term benefits and at least equal clinical outcomes, demonstration of overall cost neutrality or cost saving from the perioperative benefits is paramount in justifying the additional up-front cost.

### Current MIS Versus Open Lumbar Fusion Studies with Economic Considerations

In a retrospective comparative study, Wang et al. performed a CA (i.e., cost analysis independent of clinical outcome)

utilizing hospital charges (not actual cost) for 1- and 2-level MIS (performed in patients with unilateral symptoms) and open (performed in patient with bilateral symptoms) posterior interbody fusion for lumbar spondylotic disease, disk degeneration, and spondylolisthesis [56]. During a 14-month period, 74 patients were treated (59 1-level [75 % MIS] and 15 2-level [53 % MIS] fusions). The mean LOS for patients undergoing single-level surgery was 3.9 and 4.8 days in the MIS and open cases, respectively ( $p=0.017$ ). For those undergoing 2-level surgery, the mean LOS was 5.1 for MIS versus 7.1 for open surgery ( $p=0.259$ ). Single-level MIS procedures were associated with average charges of \$70,159 compared with \$78,444 for open surgery ( $p=0.027$ ). For 2-level surgery, mean charges totalled \$87,454 for MIS versus \$108,843 for open surgery ( $p=0.071$ ). The primary drivers for these significant differences in hospital charges were noted to be complications and associated increased length of stay. Interestingly, for single-level surgeries, 5 and 20 % of patients undergoing MIS and open surgery, respectively, were discharged to inpatient rehabilitation. For 2-level surgeries, the rates were 13 and 29 %, respectively. The economic impact of this is another potential benefit of MIS; however, the associated charges were not accounted for in this study. Due to the rather large variation in hospital charges among the small cohorts, it is difficult to make any comparisons to other institutions or reports. In a subsequent study, Wang et al. reported on a cross-sectional retrospective analysis of acute hospital cost following MIS versus open lumbar interbody fusion [29]. Using the Premier Perspective administrative database, the authors identified a cohort 6,106 patients undergoing 1- and 2-level lumbar interbody procedures ( $n=1,667$  MIS cases). The analysis was from the perspective of the hospital inpatient visit and included case costing data categorized into specific cost centers (emergency room, laboratory, operating room, pharmacy, professional fees, radiology, respiratory, room and board, central supply, therapy, cardiology, other and total cost). In this data set, the largest cost contributors were the central supply, operating room, and room and board. The adjusted analysis demonstrated a nonsignificant difference in cost for 1-level fusions (MIS \$29,187 vs. open \$29,947,  $p=0.55$ ). For 2-level procedures, the total cost was on average \$2,106 less for MIS procedures (MIS \$33,879 vs. open \$35,984,  $p=0.0023$ ). Minimally invasive surgeries were associated with greater central supply cost (i.e., implants and disposables) and typically less cost in most other categories compared to open. For 2-level surgeries, greater variance in cost associated with prolonged LOS was a significant driver of increased cost for the open cohort.

In their editorial, Deluzio et al. reported on a retrospective CA of 211 patients roughly half of whom received 2-level open posterior lateral interbody fusion (PLIF,  $n=102$ ), while the remainder had been operated via a minimally invasive

approach for degenerative conditions (specific diagnoses not reported) [2]. The MIS technique involved a lateral approach at L1–L5 and a transsacral fusion at L5–S1. The costing data was from the perspective hospital and included direct cost from the index procedure, the initial hospital stay, transfusions, reoperations, and residual events that occurred up to 45 days following discharge from hospital (ER visits, readmissions to hospital, rehabilitation). The average length of stay for the MIS group was 49 % lower than the open group (1.2 vs. 3.2 days). Overall the MIS group saved on average 2,563 USD per patient versus the open surgical group. The majority of cost saving resulted from reduced length of stay and residual events associated with the MIS cohort.

In a recent retrospective study, Pelton et al. analyzed intraoperative, immediate postoperative, and financial outcomes (cost analysis) in worker's compensation and non-worker's compensation patients undergoing either an open or MIS TLIF. Sixty-six consecutive patients undergoing a single-level TLIF (open/MIS) were analyzed (33 in each group) [67]. Twenty-four total worker's compensation (WC) patients were identified (11 MIS, 13 open). All patients had a diagnosis of either degenerative disk disease or spondylolisthesis and stenosis. WC status did not significantly impact perioperative outcome parameters in either the MIS or open groups. However, there were significant differences favoring MIS (WC and non-WC) compared to open (WC and non-WC) TLIFs in perioperative (operative time, blood loss, and hospital length of stay) and clinical outcomes (6-month pain score). Costing was determined using administrative databases and was isolated to the perspective of the hospital (direct and indirect cost including blood, imaging, implants, lab, pharmacy, allied health, room and board, and surgical services). There were statistically significant differences in total cost amounts between WC MIS TLIF and WC open TLIF (\$28,060 vs. \$33,862, respectively;  $p=0.0311$ ) and non-WC MIS TLIF versus non-WC open TLIF groups (\$29,429 vs. \$32,998, respectively;  $p=0.0001$ ). Although, for the minimally invasive surgeries, implant cost represented a higher percentage of total hospital cost (approximately 10 % higher), the difference in other health-care resource utilization compensated for this difference and resulted in an overall cost savings.

In their 2011 retrospective cohort study, Rampersaud et al. compared the direct economic impact of 1- and 2-level fusion for grade I or II degenerative or isthmic spondylolisthesis via an MIS TLIF technique compared with conventional open posterior decompression and instrumented fusion [31]. A total of 78 consecutive patients were reviewed (37 MIS and 41 open). The economic perspective of the study was from that of the hospital with direct case costing data that included operative costs, nursing (including postanesthetic care, step-down unit, intensive care unit, and ward), medical imaging, laboratories, pharmacy, and allied

health services. Costs of preoperative or postoperative rehabilitation or other outpatient health system costs were not collected. Institutional, patient, or societal indirect costs were also not collected. The groups were comparable in terms of age, sex, preoperative hemoglobin, comorbidities, and body mass index. Groups significantly differed ( $p < .01$ ) regarding baseline ODI and SF-6D scores, as well as number of 2-level fusions (MIS, 12; open, 20) and number of interbody cages (MIS, 45; open, 14). Blood loss (200 mL vs. 798 mL), transfusions (0 % vs. 17 %), and length of stay (6.1 days vs. 8.4 days) were significantly lower in the MIS group. Reported complications were also fewer in the MIS group (4 vs. 12,  $p < .02$ ). Both groups had significant improvement in 1-year outcome ( $p < 0.001$ ). However, the overall changes in ODI and SF-6D scores trended in favor of the MIS group at 1 year ( $p = 0.08$ ). Multivariate regression analysis showed that LOS and number of levels fused were independent predictors of cost. Age and MIS were the only predictors of LOS. Baseline outcomes and MIS were independent predictors of 1-year outcome. The mean total direct cost of an open fusion was 1.28 times greater than that of an MIS fusion ( $p = .001$ ).

The cost analysis of these aforementioned comparative studies (retrospective cohorts) has all demonstrated lower perioperative cost associated with MIS from the limited perspective of the hospital and the perioperative time horizon. These studies demonstrate that the additional cost associated with the index MIS procedures seems to be compensated for by reduced resource utilization in the perioperative period. The most reproducible cost saving is associated with an overall reduction in LOS and utilization of other acute postoperative resources afforded by the MIS techniques. These studies only presented hospital cost for the index procedure and did not provide ongoing health-care cost or cost of revision surgery in either cohort. Furthermore, these studies (with the exception of Rampersaud et al. [31]) did not take the clinical outcome into account and thus represent cost analysis. If we consider the current comparative evidence on clinical outcome presented in Table 3.2 and make an assumption of clinical equipoise, these data can be considered as cost-minimization analyses (from the limited perspective of the hospital) that demonstrate cost savings in the perioperative period.

In addition to a cost analysis, Rampersaud et al. also performed a CUA to assess both cost and clinical outcome using the SF-6D at 1 year to determine the QALYs gained by each group [31]. The mean total direct cost was \$14,183 CAD for the minimally invasive group compared with \$18,663 CAD for the open group. The pre- and postoperative change in health utility was significant for both groups ( $p < 0.0001$  for MIS and  $p < 0.003$  for open) at the 1-year mark with a gain of 0.113 (SD=0.10) and 0.079 (SD=0.08) QALYs for the MIS and open groups, respectively. The cost/QALY was \$128,936 for MIS and 232,912 for open

(unadjusted for differing number of levels between cohorts). The authors did not perform an assessment of the incremental cost-utility (ICUR) between MIS and open fusion on the basis that a CEA (ICER/ICUR) typically makes the assumption that the new strategy is likely to cost more but has a clinically greater effect. In this case because the new strategy (MIS) costs less or is at least equivalent (using sensitivity analysis) and has a greater yet statistically and likely clinically insignificant difference in effect on the outcome, the MIS technique would be at the very least cost neutral [20]. However, due to the limited 1-year time horizon, the cost-utility of both techniques was over the \$100,000 per QALY threshold to be considered reasonable value. The authors provided an estimate of the cost-utility for each group if the outcome was sustainable at the 2- and 4-year mark. As expected for the method of QALY determination, the cost/QALY significantly decreased for both groups to a more favorable value (MIS, \$37,720; open, \$67,510). In a recent study, Rouben et al. reported the outcomes of 169 consecutive patients with a minimum of 3-year follow-up after 1–2-level MIS TLIF for a variety of spinal diagnoses [68]. At a mean of 49 months, the average improvement of the ODI (41 %) score was sustained. In addition the reported revision rate was 14.2 % (7.6 % for symptomatic instrumentation, 1.8 % for adjacent segment disease, 0.6 % for infection in one patient, and 0.6 % for a pseudoarthrosis in another patient). Although for different indications, this revision rate is similar to that reported for the SPORT trial data at 4 years [15–17]. A current longer-term series from the principal author (manuscript in preparation) has demonstrated similar findings that support the results reported by Rouben et al. [68]. Simon and Rampersaud have recently presented a cohort of 66 patients with a minimum of 2-year follow-up after MIS TLIF for low-grade degenerative or isthmic spondylolisthesis. In 27 patients with 5-year follow-up (90 % follow-up rate), the improvements in ODI and SF-36 seen at 2 years were maintained at the 5-year mark [69]. These results support the inference of the projected CUA performed by Rampersaud et al. [31].

In addition to procedural durability, a more accurate HEE requires the capture of other ongoing cost following discharge from hospital. No current study has assessed ongoing resource utilization beyond the perioperative period following MIS versus open spine surgery. As demonstrated in the recent CEA analysis from the 4-year SPORT data, ongoing cost, especially indirect cost, is significant following intervention for spinal disorders [14]. This was particularly noted for the degenerative spondylolisthesis (DS) subpopulation, where the largest ongoing cost occurred in the nonoperatively treated patients. Sustained clinical superiority and reduced ongoing cost enabled the ICUR for the surgically treated DS group to improve from \$115,600 at 2 years (above 100 K cost-effectiveness threshold) to \$64,300 per QALY at 4 years compared to nonoperative treatment. If the clinical



outcomes are similar as in the case of MIS versus open surgery, then one has to make the invalidated assumption that ongoing health-care utilization may be similar, until data supporting this assumption is obtained. In the interim, more costly adverse events such as deep surgical site infections and revision surgery (in the short or long term) for other causes (e.g., instrumentation-related pain, pseudoarthrosis, or adjacent segment degeneration) should, at the very least, be accounted for in MIS versus open lumbar fusion HEE models. Two recent reviews suggest that ongoing medical cost may in fact favor MIS. In the first study, Parker et al. aimed to determine the incidence of surgical site infections (SSI) in patients undergoing MIS versus open TLIF reported in the literature and the direct hospital cost associated with the treatment of SSI following TLIF [65]. Ten MIS TLIF cohorts (362 patients) and 20 open TLIF cohorts (1,133 patients) reporting incidences of SSI were identified. The cumulative incidence of reported SSI was significantly lower for MIS versus open TLIF (0.6 % vs. 4.0 %,  $p=0.0005$ ). At the institutional level, 120 open TLIF procedures, SSI occurred in six (5.0 %) patients. The mean hospital cost associated with the treatment of SSI following TLIF was \$29,110 in these six cases. The authors determined that the 3.4 % decrease in reported incidence of SSI for MIS versus open TLIF corresponds to direct cost savings of \$98,974 per 100 MIS TLIF procedures performed. In the second study, Wu et al. performed a meta-analysis looking at fusion rates between MIS and open TLIFs [64]. As noted earlier, the authors demonstrated equal fusion rates between MIS (94.8 %) and open (90.9 %) TLIFs. The authors also reported a difference in reported adverse events favoring MIS (7.5 %) versus open (12.6 %).

The assessment of indirect cost and in particular productivity (e.g., return to work and reduced out of pocket expenses for care givers and house work) is grossly absent in the MIS fusion literature. Given the aforementioned findings, if additional economic benefits exist for MIS of the spine, the impact on improved productivity and other indirect economic benefits (i.e., from the societal perspective) is where we should be able to demonstrate it. With a demonstration of cost savings in the perioperative period, the promise of reduced morbidity from MIS of the spine to enable quicker return to activity, while many believe it to be true (the principal author included), needs to be objectively assessed and the economic impact quantified. It is here where the true cost-effectiveness of MIS of the spine may garner the greatest support.

### Conclusion

Health-care systems are constantly changing and introducing necessary reform in an attempt to meet clinical demands, while keeping growing financial concerns in check. Regardless of what changes occur in health reform, resource allocation will likely favor those interventions that demonstrate the best value. In order for clinicians

to contribute to meaningful reform, insight into the decision-making language (e.g., HEE, cost per QALY gained) of the government, payers, and policy makers is crucial. For the diagnostic categories of lumbar disk herniation and spinal stenosis without and with spondylolisthesis, open spine surgery procedures have shown both clinical efficacy and cost-effectiveness at 4 years compared to nonoperative treatment. Current comparative data (albeit of overall low evidentiary quality) suggest that MIS lumbar fusion provides at least equivalent clinical outcome in the midterm (1–2 years) and consistently demonstrates quality and cost-benefits in the perioperative period compared to open fusion. The initial increase in direct procedure-associated cost of MIS fusion appears to be offset by the perioperative benefits which produce an overall net cost savings. However, the evidence is sparse and of poor quality to enable any strong conclusions of superiority of MIS versus open. Going forward, more comprehensive HEE comparing the outcome effect size over time, the potentially lower post-surgery ongoing medical resource utilization and perhaps most importantly the difference in indirect cost such as earlier return to activity (i.e., productivity) of MIS versus open spine surgery are required to support a broader adoption of MIS of the spine from a societal and payer perspective.

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