

## ABSTRACT

The Anesthesiologist's Responsibility to the Market: An Economic Analysis of Intravenous and Inhalation Anesthesia's Effect on Patient Cognitive Outcomes

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Spending on anesthetics in the healthcare market has steadily increased with little to no evidence of proportional improvements in patient outcomes. Investigations into this phenomenon illustrate that the effect of common complications are often minimized in treatment plans. Using QALY (Quality Adjusted Life Year) metrics and data on the frequency and cost of Post-Operative Cognitive Dysfunction, this research presents a comparative analysis of inhalation and intravenous general anesthesia methods. Each method is analyzed for their respective opportunity costs to the patient and to the greater healthcare system. The economic impact of Post-Operative Cognitive Dysfunction (POCD) for both anesthetic methods is discussed to highlight the long-term costs that are typically neglected in the healthcare market. Finally, this thesis suggests an economically efficient course of treatment, examining the role of the clinician in advocating for cost-effective healthcare options in surgical care and evaluating the various policy approaches to minimizing costs while maximizing care.

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THE ANESTHESIOLOGIST'S RESPONSIBILITY TO THE MARKET: AN  
ECONOMIC ANALYSIS OF INTRAVENOUS AND INHALATION ANESTHESIA'S  
EFFECT ON PATIENT COGNITIVE OUTCOMES

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## CHAPTER 1

### An Introduction to Anesthesia Cost Implications & Post-Operative Cognitive Dysfunction

The three goals of the healthcare industry are consistently agreed upon as increasing access, improving quality, and maximizing cost efficiency. Despite these intentions, healthcare spending continues to skyrocket, totaling over 20% of the Gross Domestic Product in America. Much of this is attributed to waste in administrative costs, lack of available information for consumers, lack of incentives for decreasing costs, and a poorly designed insurance system. Since the year 2000, the amount of anesthesia stipends has risen over 400% (O'Neill, 2017). However, the improvements in quality of patient outcomes have been marginal in comparison. Few have been asking questions regarding the efficiency of patient outcomes in anesthesia despite the cognitive risks associated with it.

Post-operative cognitive dysfunction or post-operative cognitive decline is a 'functional impairment of the nervous system activities, such as memory, executive function, language, direction, emotion, visual space structural ability, in patients after surgery/anesthesia, which is a kind of reversible mild cognitive impairment (MCI), (Jun Liu, Binbin Zhu, frontiers article 1). The primary symptom that is observed throughout recovery for patients is challenges in short term memory. While a reversible condition, the time frame of recovery is understudied and often underestimated, leading to patients suffering in their day to day lives. Patients are typically without proper warning from surgeons regarding how this may affect their livelihood and without a clear treatment

plan should they develop POCD. This means that many patients do not fully understand the cognitive risks of surgical intervention and are ill prepared for the potential recovery process as a result. There is also research that finds if evidence of Mild Cognitive Impairment is present immediately following surgery, it is a strong indicator that the patient will continue to struggle with cognitive impairment in their recovery process and beyond. This accelerated mental decline is known to develop into more serious cognitive decay for elderly patients, demonstrating that in some cases, full recovery is not possible. Especially for patients with a high propensity to develop other cognitive impairments, like Alzheimer's or Dementia, this rapid cognitive decline can be a substantial setback to their quality of life remaining.

The disordered mental functioning that often arises after surgery can be life-altering, impacting patient's ability to learn new information, guard against attention deficits, and prevent executive function impairments. In the existing research, Post-Operative Delirium and Post-Operative Cognitive Dysfunction are often discussed similarly despite being distinct disorders. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) sees delirium as "a disorder of reduced attention and orientation to the environment, accompanied by cognitive disturbances in an acute and fluctuating course with lucid intervals" (Safavynia, 2019). Delirium typically occurs immediately following surgery with most cases lasting for a week or less. This is strikingly different from POCD (primarily dealing with short-term memory function deficits), which will be discussed in this thesis. Official diagnosing definitions for this disease have been fluidly changing for the past years, but some agreement has been made

in recent years. The defining of the cognitive impairment can be differentiated by the time of onset with preoperative designating conditions pre-existing to the operation and postoperative emergence for early intra-hospital phases of recovery. For conditions lasting longer than 30 days with delayed cognitive recovery, that is, the standard postoperative neurocognitive disorders known as POCD or NCD (neurocognitive disorder) for up to one-year post surgery (Germany). For the purpose of understanding the shift in definitions over time, it is beneficial to examine how these standards were agreed upon.

The analytic criteria for identifying and measuring Post-Operative Cognitive Dysfunction is neither straightforward nor consistent, creating barriers to progressing in understanding the frequency of its occurrence. This type of cognitive change following surgery gained more traction in literature in the 1980 as studies began to use in depth testing to measure its occurrence, finding that “cognitive changes have been identified up to 7.5 years afterwards,” (Evered, 2018). Studies recording the prevalence of this condition incentivized researchers to gain more information to better equip patients and physicians. As more literature emerged, there also grew a need for consistent nomenclature and diagnostic criteria to minimize confusion. This consistency of nomenclature would allow for better management of patients and better communication among care teams, an essential component of care for an aging population undergoing surgical intervention.

For the majority of this topic’s prevalence in literature, Post-Operative Cognitive Dysfunction has been studied isolated from cognitive studies occurring in the general

population, further complicating the journey to clarity in diagnostic criteria. The work by Evered et. al suggests that “the diagnostic criteria for the cognitive changes associated with anesthesia and surgery detected by psychometric testing should not be differentiated from neurocognitive disorders (NCD) in the general population,” (Evered, 2018). This study used the Delphi approach, collecting opinions from a variety of experts to reach consensus. This would enable the DSM-5 to be used in its present editions and more accurately measure the POCD occurring. Further, this small clarity in how testing for this condition is conducted would allow for different researchers to make strides that collaborate with each other instead of being distinct voices that overlap in concepts, but cannot truly merge data or results well. This study’s dedication to developing consistent diagnostic criteria for the clinical community acknowledges the nuances to this research with a refreshingly cautious view for the research being published and conducted.

Just eight years prior, data illustrates the benefits of these standardized practices for diagnostic progress and research validity. A study from 2010 by Rudolf et al investigated variability in measurement of POCD in cardiac surgery, looking into sixty-two studies. By investigating the methods used to collect data, they found that attention and memory were properly measured most frequently, but a variety of other cognitive domains were captured in staggeringly inconsistent levels. Due to the lack of uniform measurement standards for POCD, validity of results in this field are inherently questioned. If there is not a clear diagnostic path, understanding the range of impact this condition has on patients is nearly impossible. This study abstracted the patient testing and compared it to the 1995 Consensus Statement to illustrate the shortcomings. There



have been clear impediments to progress in understanding this field in further dated literature, though improvements in diagnostic tools, standards, and clinician attitudes towards POCD have reduced this concern over the years. This study highlights the importance of research in this field being broadened to having more standardized checks into the mental recovery of patients following operative procedures. These checks would have to include baseline checks prior to surgery and a clear measure for what kind of disturbances in cognitive performance are considered significant due to the volatile nature of our cognitive function in response to things like sleep, activity, etc. This simple step could be revolutionary in both researching the frequency of this complication occurring but ultimately in its prevention and treatment. If a problem is properly measured over time, it becomes much easier to tackle for clinicians, patients, and policymakers alike.

Studies have also demonstrated the links that exist between the pathophysiology of Post-Operative Cognitive Dysfunction and early stage Alzheimers. A prospective, randomized study conducted on mice found the same hallmark characteristics, including, “microgliosis, astrogliosis, enhanced transcriptional and translational activity of beta-amyloid precursor protein, and  $\tau$  protein hyperphosphorylation in the hippocampus,” (Wan Y, et. Al). This evidence suggests that patients with a propensity towards developing Alzheimer’s could be at a higher risk for developing POCD if the means of development are physiologically in alignment. This further alludes to the possibility that anesthetics used are imperative to be closely investigated for the potential longevity of patient’s cognitive function. It additionally raises the question of if surgical intervention

requiring anesthesia could accelerate the development of these cognitive impairments, minimizing the optimal years a patient has left. This hole in research is another key question that researchers should aim to investigate to fully understand the costs associated with the benefits of surgical intervention.

The strongest risk factor for developing Post-Operative Cognitive Dysfunction is age, which is also strongly correlated with more necessary surgical operations that require anesthesia (Safavynia, 2019). This compounding problem is further exasperated by the aging population that healthcare must learn to optimally serve. The very population that demonstrates the highest risk for Post-Operative Cognitive Dysfunction is the same population that is most likely to undergo surgical procedure and require anesthesia for this to occur. While altogether often underestimated by patients and physicians, this seemingly simple ailment has staggering effects on the healthcare economy in the official and unofficial treatment for these patients and their long-term outcomes. Is there a simple way to reduce the frequency or severity of this risk? How can we better prepare physicians and patients to make decisions about their operations that reflect the true opportunity cost at stake?

Scientists agree that while the investigations into the true epidemiological cause of POCD have yielded inconclusive results, the main suspect for this is neuroinflammation. Prior studies have begun to understand the association between surgery and POCD, but there is still a lack of conclusion regarding the pathogenesis of POCD; some theories cite a weakening of the blood-brain barrier being the mechanism by which neuroinflammation and the neurodegenerative diseases associated with it to

thrive (Safavvnia, 2019). The proposed associated surgical causes for Post-Operative Cognitive Dysfunction include length of surgery, low levels of perfusion or low perfusion time, hypoxia, low arterial PaCO<sub>2</sub>, etc., (Matlar C.E. Porportion). These surgical operative risks should be minimized in light of their correlation with POCD and regardless of their causation of POCD, proving to be influential in predicting the long-term recovery and health of a patient. For coronary bypass surgery patients in their 70s, as many as 60% experienced this decline in cognitive abilities (10-13 from Matlar). This number is far from insignificant and out of proportion with concerns for the associated cost burden of this same prevalence. But what implications does this have?

A study in 1998 known as “The International Study of Post-Operative Cognitive Dysfunction” looked at over 1200 patients 60 years of age and older, investigating the perioperative neurocognitive disorders occurring in non-cardiac surgery (Moller JT, Cluitmans P, 1998). This study found delayed neurocognitive recovery in 25% of patients one week after surgery and postoperative neurocognitive disorder present in 10% of patients three months following surgery, with age being the most significant risk factor for the three-month continuation effects. This study demonstrates the prevalence of Post-Operative Cognitive Dysfunction in elderly patients. While there is a higher rate for POCD in patients who have undergone cardiac surgery than those who have undergone non-cardiac surgery, the rates found in The International Study of Post-Operative Cognitive Dysfunction demonstrate that the prevalence of this complication is undeniable (Damuleviciene, 2010). With such a significant problem, the lack of measures in place to

properly educate patients on measures for prevention and treatment or incentivize researchers and clinicians to improve these statistics is alarming.

In addition to the surgical complications and recovery process being longer for patients with POCD, studies have also demonstrated the more serious effects that can arise. A longitudinal study of cognitive recovery after major noncardiac surgery found that elderly populations are not only more likely to develop POCD following surgery, but also have significant increases in rates of mortality for those who do develop this complication (Monk et al, 2018). They found that patients who exhibited symptoms of Post-Operative Cognitive Dysfunction following surgery were more likely to die in the first three months following surgery and those who still exhibited symptoms of POCD three months following surgery were more likely to die in the year following surgery. This study demonstrates that while POCD can be viewed as a less serious complication due to its “invisible” nature, it is correlated with severe detriments to health in the recovery process. This study found these results with p-values of 0.02. With these kinds of costs being neglected in decision making for surgical intervention, there is a clear gap in what literature suggests and what clinicians are practicing.

Anesthesia for major surgery typically involves one of two, or both methods of drug: inhalation or intravenous. The different methods of delivery also typically have different drugs used, different costs associated, and potentially different outcomes for patients at high risk for Post-Operative Cognitive Dysfunction. By evaluating both options for their monetary cost and also for their opportunity cost of use for the long-term care of the patient, a path for significant improvement in the efficiency of anesthesia

healthcare can be forged. There is little research currently evaluating more than the existence of Post-Operative Cognitive Dysfunction, so this extension of the research to ask about different methods and outcomes for reducing the overall cost associated with each is vital to making informed policy decisions.

The emergence of TIVA (total intravenous anesthesia) was revolutionary for the field of anesthesia. Inhalation anesthetics have been used for maintenance of sedation throughout surgery, but the use of Propofol TIVA could be the basis for more rapid recovery. The primary advantage to inhalation anesthetics being used for the duration of surgery is found in the sophistication of equipment and ability to precisely control the anesthetic state at a relatively low cost. Children tend to prefer induction with inhalation methods of anesthesia due to more prevalent fear of needles, but many experience increased claustrophobia associated with inhalation anesthetics. Intravenous have the advantage of being distributed rapidly through the central nervous system. However, there are many clear advantages to inhalation anesthesia for the duration of surgery due to more sophisticated devices being available for measuring the level of anesthesia and maintaining this number throughout surgery.

Healthcare economists recognize the important role that incentives play in creating changes in behavior. With what we know regarding Post-Operative Cognitive Dysfunction and its harmful effects on patient's lives and healthcare spending, it is essential that questions about the most effective decision for patient outcomes are less riddled with information asymmetries. Patients typically have little to no choice or background information regarding the types of anesthesia available and this is typically

not their main focus when educating themselves on the surgery they are to receive. This can lead to patients unknowingly being treated with anesthetics that have higher rates of cognitive decline and ultimately lead to them being unsure how to best treat this unanticipated problem.

Due to the informational asymmetries, patients are effectively unable to properly manage risk in their decision making which could further perpetuate the excessively inefficient spending in the healthcare market. When surgical trauma is not limited to the surgical site, the efforts towards recovery cannot be limited to the direct results of operation. Patients at greater risk for these costly cognitive impairments have the right to understand fully the potential costs for their health.

## CHAPTER 2

### Comparison of Anesthetics for Patient Outcomes

In order for cost-benefit comparisons to hold any weight in healthcare economics, the patient outcomes must be considered alongside the monetary costs of administering and acquiring the drugs in question. A variety of studies have measured aspects of these anesthetics' outcomes in various surgical types. The research literature surrounding elderly patient outcomes for intravenous and inhalation anesthesia will be compiled and compared for rates of surgical complications, focusing on Post-Operative Cognitive Decline. While this thesis is focused primarily on the cognitive outcomes of patients, the other side effects that are frequent complaints and cost drivers for anesthetics will also be examined here for a more holistic review that allows for a more comprehensive cost-benefit analysis to be considered. The critical review of this research will make an argument for which anesthetic method produces the best patient outcomes by minimizing unnecessary trauma. This chapter creates the outline for then evaluating economic cost implications to be estimated in chapter 3. These values still do not include the long-term burden associated with POCD or the potential additional cost that the risk of this condition developing further incurs.

A study performed by Miller et, al, 2018, found evidence that maintenance of anesthesia with intravenous Propofol reduced Post-Operative Cognitive Decline in elderly patients undergoing non-cardiac surgery. This study investigated the use of intravenous versus inhalation anesthesia for postoperative cognitive outcomes in elderly

people undergoing non-cardiac surgery by searching the Cochrane Central Register of Controlled Trials. The study narrowed to 7 randomly controlled trials with participants over 60 years of age who would undergo non-cardiac surgery in which they were able to find low-certainty evidence demonstrating that maintenance with Propofol-based TIVA reduced POCD. The study selected the most reliable studies for internal and external validity when choosing their combined data. This study, as many of the studies that will be investigated in this thesis, was limited from the inherently unfeasible nature of blinding anesthesiologists to study groups. Many studies also had to be removed from data consideration due to high rates of attrition bias or high risk of selective reporting bias. This study noted that the continued investigation into comparing these two methods could be influential in further solidifying certainty of their conclusions.

A free-flap surgery study also investigated the difference in outcomes between patients who underwent surgery with inhalation or intravenous anesthetics. This study looked at one-hundred and fifty-six patients retrospectively divided into their anesthetic type pools that were then tested for balancing metrics (Chang et al., 2016). This study found that individuals who had surgery with TIVA had fewer pulmonary complications with a p-value of 0.0008. The study theorized that this could be due to lower perioperative fluid requirements for the TIVA group. The main concern in studies such as these is that there is no mention of how anesthesiologists are deciding between the two types of anesthetics for these patients, which could mean there are inherent differences in the two groups leading to these results. While balancing metrics are used, it is unclear



how bias is managed when there is not an explicit understanding of the decision-making process for the treatment plan for these patients mentioned in the literature.

A study also utilized the metric of QoR-40 to compare the results for the two anesthetics. QoR-40 is a measure of qualitative recovery that is used in clinical literature and incorporates five dimensions of health: patient support, comfort, emotions, physical independence, and pain with a score range of forty to two-hundred. This kind of holistic evaluation is excellent for considering cost-benefit estimates of these treatment options. The study examined 156 records with 922 total patients in their meta-analysis. They found a significant increase in QoR-40 score for Propofol based TIVA on the day of surgery with the main dimensions of impact being physical comfort, emotional status, psychological support, and physical independence (Shui, 2021). This study did not find conclusive evidence of there being significant differences between the two anesthetics over extended time frames and suggest further research for improved certainty. The metrics used in this study encompass factors that are typically influential in hospital discharge times and patient perception of care.

A study conducted by Kampmeier found there to be significantly lower post-operative nausea and vomiting rates in addition to less time spent in the PACU. The claim made of Propofol being the dominant economic strategy for physicians in both inpatient and ambulatory surgery centers is further strengthened by the significant overall cost difference compared to inhalation anesthetics did not consider the reduction in prices, meaning the calculated difference is in fact larger in practice. The study had multiple strengths, including several robustness checks and following formulas suggested

in the *Cochrane Handbook for Systemic Reviews of Interventions*. This study did note that there was increased respiratory recovery time with intravenous, but it was deemed not clinically relevant. This type of conclusion is an example of situations where using a less monetary cost-effective anesthetic intervention could be more beneficial for an individual, demonstrating the economic importance of specialized care.

A further study was performed to research elderly noncardiac surgical patients for the incidence of Post-Operative Cognitive Dysfunction (Pang, 2021). The meta-analysis saw an average decrease of 22 percentile points between means of POCD incidence in days 2-6 after surgery, favoring intravenous Propofol anesthetics over inhalation methods. This time period has been demonstrated to be critical for the continuation of POCD in patients and is a strong indicator for the rest of their recovery. This study had many strengths, including 1854 patients being included in the study and moderately significant p-values (0.025). They also noted lower systemic inflammation in patients who were treated with Propofol. While an increased sample size and more consistent metrics of measurement for evaluating the cognitive status of patients is encouraged to strengthen these results, they still demonstrate a trend that has been continually emerging in literature with studies of this kind. The peripheral inflammation mentioned is important because this will increase the permeability of the blood-brain barrier and increase likelihood of unnecessary neurological trauma.

One study also examined the impact of inhalation vs intravenous anesthetics on delayed neurocognitive recovery in elderly patients following cancer surgery (Zhang et al., 2018). This study had strong controls for how cognitive functioning was assessed

before and after surgery in addition to controlling for age and education controls. This study also uses the delayed neurocognitive recovery definitions reviewed and recommended in previous chapters of this thesis. In this randomized controlled trial, the incidence of delayed recovery was 14.8% lower for patients in the Propofol group than in the inhalation group. This is yet another example of these results being repeated with the same cognitive impacts being observed. This study is also an excellent model for further research recommendations in this field.

In addition to these studies detailing the comparison of inhalation and intravenous anesthetics for their impacts on cognitive recovery, some studies have chosen to examine the sleep quality patients experience following surgery because it is a vital component of healing. In 2021, seventy-four patients were randomly assigned to intravenous or inhalation anesthetics for laparoscopic surgery and then monitored for sleep quality on the night before surgery, the first night after, and three nights after. Participants were also evaluated for postoperative complications. This study found that sleep efficiency was increased post operation, there was lower postoperative nausea and vomiting, lower dizziness, and less post-operative pain for patients in the Propofol group than in the inhalation group (Li et al., 2021). Sleep efficiency was measured through tracking REM cycles with a Wireless Portable Sleep Monitor. All differences were considered significant with a p-value of 0.05. This study was limited by sample size, but the results are very promising for the consideration of intravenous and inhalation anesthetics having significant differences in recovery for patients. The extension of this study to further

populations receiving different types of surgery and to see if results are reproducible is highly recommended.

Preventative care has long been known to be a major way to drive down costs in the clinical setting and this should include considering treatment alternatives with individual propensities for potential risks being taken into consideration. The everchanging field of healthcare should demand clinicians prepared to make these types of informed decisions to maximize the efficiency of their care. When the use of a certain technique is not only more beneficial for patients, but also most efficient for the cost-bearers of the market, it is only logical that this would be standard practice.

In the literature present, patient outcomes consistently note Propofol as the anesthetic method with lower rates of complications and more effective rates of healing. The recent surge in literature surrounding comparing outcomes for these two anesthetics indicates that inhalation anesthetics now has a true competitor in the market. While TIVA has long been considered to be the more expensive option, with the data emerging regarding lower rates of complications, it may be possible to see a cost-benefit ratio that strengthens the case for Propofol further. This will be examined further in the following chapter discussing costs for the treatment options.

## CHAPTER 3

### Cost Comparison

In this chapter, the findings of the research assembled will be used to create a recommended care plan for anesthesiologists and healthcare administration to consider implementing. This section will be focused on how the information presented in the prior chapter should impact the decision-making process due to the estimated economic consequences of the patient complications (calculating through referencing health and retirement longitudinal studies and known average QUALY values for these diseases). By examining these critically with respect to the cost of the medication administration, a more comprehensive cost-comparison estimation will be considered. The question of whether clinicians, patients, or administrative staff should be the most incentivized to act in response to research in this area will also be discussed here.

As demonstrated earlier in this paper, the costs of differing anesthesia methods go far beyond the operating room in which they are utilized. Oftentimes, doctors are faced with decisions for patient care that put the economic implications of treatment at opposition with the potential benefits implemented by a course of action. In the case of the data provided in the prior chapter, intravenous anesthesia can likely significantly reduce the cost of patient care and recovery complications when compared with inhalation anesthetics in similar cases. While every case is different, some trends did become apparent from the literature review conducted. Based upon this, the recommended care plan for physicians should shift. While it is costly to educate

physicians to such a high degree of specialization and individualization in their care, this paper illustrates that the benefit of this degree of training could significantly impact the lives of patients in addition to benefiting the spending level of the healthcare sector as a whole.

A study published in 2021 by Kampmeier et al. developed a pharmoeconomic model to compare overall cost rates for intravenous Propofol anesthesia and inhalation anesthesia. The models used surgical data from US patients in a meta-analysis of randomized controlled trials. This model saw that by just considering the complication of postoperative nausea and vomiting risks, Propofol TIVA significantly reduces overall costs in inpatient and ambulatory surgical settings. The cost-benefit comparison found that while there were higher costs for anesthetics, analgesics, and muscle relaxants with TIVA the reduction in PONV, time in post-anesthesia care unit, and need for rescue antiemetics led to an overall cost reduction of 11.41 USD per patient. While this number is small, the multitude of surgeries conducted each year would make this cost-savings significant in the long run. This study additionally does not encompass many of the other complications that have been noted earlier in this thesis to be significantly reduced with use of Propofol. Further, this study does not encompass the additional cost burden of Post-Operative Cognitive Dysfunction, which has been demonstrated to have a significant impact on spending. The pharmoeconomic model developed in this study could be particularly useful if extended to this cognitive complication to further solidify recommendations for intravenous anesthetics.

It must be considered that TIVA is frequently cited as having higher direct costs to implement in patient care. While this was significant in the beginning of this drug option being available to clinicians, developments in technology and reduction in transaction cost are fast-paced. It is estimated that the cost of Propofol from 2006-2019 in the United States decreased approximately 25.5% (Fresenius). This change in the average cost for administering Propofol is significant for considering studies conducted using data prior to these shifts as they fail to properly estimate the cost of the anesthetic method moving forward in clinical settings. It also may indicate trends for future cost decreases to be found in the use of intravenous anesthetics. The benefits noted in this thesis of using Propofol over inhalation anesthetics should also further incentivize physicians and researchers to seek low cost methods for implementing and manufacturing this drug.

A study was conducted in Germany to calculate the potential yearly cost of POCD in the long-term care insurance. Inpatient operation and procedure codes (OPS-codes) were used for calculations and combined with known POCD incidence rates from a BioCog study. The study also conducted numerous conservative sensitivity analyses to control for uncertainties. The data came from over 1000 patients in Germany and the Netherlands aged 65 and above who underwent a major elective surgery with general anesthesia. In their estimation, POCD related annual costs in German long-term care insurance account for approximately 1.6 billion EUR (Weber et al., 2021). This study was groundbreaking for recognizing the severity of this condition on the economy and on the healthcare outcomes of patients undergoing surgery. However, in order to improve

the healthcare outcomes (and with them the level of spending for maintaining patient health), we must uncover a comparative analysis of different anesthesia methods to have the highest chance for a cost-effective plan. Much of the cost implicated by POCD in the Germany study was not from additional inpatient costs in the case of delirious patients, but for patients exhibiting premature dependency due cognitive impairments. The long-term care burden has seldom been addressed in literature to date, nor has the unofficial cost burden of this all too common ailment.

While seeing the clinical ramifications of different anesthetics provides insight into the physical costs of each, as this paper has discussed, calculating the long-term cost of Mild Cognitive Impairments is complex. In order to get a better picture of this, Quality Adjusted Life Years (QALY numbers) will be used. A QALY is a metric used worldwide that will “account for the impact of a health state on both quality and quantity of life,” (Lawrence, 2020). The calculation for a QALY includes taking the change in utility by an action multiplied by the duration of the action, a relatively simple procedure that requires a vast level of prior calculation to arrive at those variables in the equation. Utility of a level of cognitive functioning could vary greatly from patient to patient. Despite the apparent challenges, the use of the QALY allows for a more holistic understanding of the burden of a disease in addition to the potential benefit of a treatment, budgeting the economic cost into a more digestible unit for the reader to understand.

The development of Post-Operative Cognitive Dysfunction in elderly patients is significant to their ability to live independently for the remainder of their life. POCD is



is commonly classified as a mild-cognitive impairment, or MCI. A study conducted through the Mayo Clinic Study of Aging estimated that mean medical costs for mild-cognitive impairments (MCIs) total \$6784 USD annually (Leibson et al., 2015).

Ambulatory, or outpatient care is the primary cost driver for the difference that is present between MCI and cognitive normalcy, however the further costs incurred with any more severity of cognitive decline are then primarily due to inpatient, long-term care. This is in alignment with what was demonstrated in the study of cost-burdens of MCIs in Germany. Cases of MCI in elderly patients frequently deteriorate to cases of Alzheimer's that will require intensive healthcare over time as the disease develops. Spending on these diseases is projected to increase six-fold from 2014 to 2050, illustrating the further need for preventative efforts. The increase in direct healthcare costs for an individual with normal cognitive functioning and an individual with mild cognitive impairment was also similar in value to those calculated in the previously referenced German study. Both of these studies found there to be only mildly significant differences in the outpatient care received, but both argued for higher indirect costs being incurred.

While those studies suggest an outlook on the impact of MCI for older populations, another study by Zhu et al. investigated the effects of MCI on a slightly younger population group (ages 55-90). This found a marked increase in baseline average annual direct medical cost per person (\$2969-6499 USD with the development of MCI). This is logical considering that the value of human capital in the form of cognitive function exhibits some changes in marginal returns over time as individuals age into retirement and as individuals gain experience in their careers, etc. Some of the most vital

years for an individual to exhibit high cognitive function occur earlier in life as the returns on cognitive functioning diminish over time past a certain peaking point in one's career. Learning is easier when one is young and more economically useful leading up to the prime of one's career. The marginal return to possessing these cognitive abilities is higher earlier on in one's life as a result. However, this varies from individual to individual indicating the level of heterogeneity that can occur in educational and career ambitions.

A study conducted by Xiong et. Al in 2021 looked into the Quality Adjusted Life Expectancy for Mild Cognitive Impairment in individuals aged 45. Their data was gathered from both the National Cause of Death Monitoring Data and the China Health and Retirement Longitudinal Study (CHARLS), in which they were able to use individuals with cognitive impairment and multimorbidity and compare them with those with cognitive impairment alone or multimorbidities alone to estimate each of these factors respective impact on an individual's quality of life. This study found that the combined effect of cognitive impairment and multimorbidity was 7.61 years, and 3.53 years for cognitive impairment's effect alone. This study additionally controlled for self-reporting chronic conditions in which memory impairments could create overlapping estimates in their analysis. There were also additional reductions in quality of life found when investigating the effect on the population as a whole, a value particularly interesting for the implications among those with neither condition. POCD is demonstrated to truly be a public health issue by this additional metric illustrating its wide-reaching impact. This study is one of many advocating for further emphasis on this field of research and

further investigation into the interventions that could be taken at an earlier time, especially for populations at risk.

The level of economic burden associated with a QALY value has been set between 50,000 and 100,000 USD by the Institute of Clinical and Economic Review. QALY metrics and their use in evaluating drug effectiveness have been under scrutiny for potentially underestimating the ability of drugs to create positive impacts if the QALY added is under a year. For example, a terminally ill patient being offered a drug that could provide additional months of life could see this benefit as holding much more value than an individual at perfect health. If solely the QALY metric is used in determining the drugs coverage rates among insurance, both individuals will not receive coverage and may likely not access the drug as a result. Acknowledging the shortcomings and dangers of this metric is important, but the use of the QALY is still highly applicable for evaluating the impact of complications that can arise from a course of treatment. Anesthetics for necessary general surgery are not often called into questions of necessity by insurance companies. However, treatment for minor cognitive impairment can be complex to navigate for patients relying on Medicaid or Medicare, where inpatient hospital care is not necessary until the condition develops further.

If the monetary values agreed upon for a QALY are applied to the metrics found in the Xiang et. Al. study, the range of economic burden for each individual affected by POCD without the impact of other conditions is \$176,500-\$353,000 USD. If the patient has other compounding conditions present, as the majority of patients requiring surgical intervention are, then the estimated economic impact to each patient of suffering from

Post-Operative Cognitive Dysfunction would be \$380,500-\$761,000 USD. These numbers are estimates only as there are concerns for external validity of a study conducted on a different population, but they illustrate the severity of this condition in light of the unawareness that patients have of the risk for this condition when electing for surgical intervention.

Medicare spending is also notably impacted by post-operative neurocognitive disorders as well as commercially insured populations. A retrospective cohort study examined claims data from the Bundled Payments for Care Improvement Advanced Model to measure inflation-adjusted Medicare post-acute care payments tied to developing a post-operative neurocognitive disorder. The study found that nearly two percent of individuals were diagnosed with a cognitive impairment following surgery (Boone et al., 2020). The presence of new neurocognitive disorder for the year following surgery was associated with a \$17,275 USD increase in costs for Medicare patients. Demonstrating that this risk is of high importance to government spending further shows the importance of policymakers considering its impact. This study is yet another calling for cognitive recovery of surgical intervention to be a target for lowering costs and promoting value-based care.

The literature continues to strengthen the case for intravenous anesthetics from both a clinical and economic standpoint. The potential cost burdens of cognitive decline will continue to rise with an aging population if inefficiencies and preventative care are not addressed. The pursuit of holistic health requires physicians to consider the elements of economic responsibility in healthcare spending in addition to patient outcomes from

treatments. The research presented shows that physicians can minimize costs by maximizing patient care in selecting an anesthesia method. The literature review presented in this thesis shows that this form of preventative care should be advocated for in further research and clinical settings. For some patients, the burden that these complications pose could outweigh the marginal benefit that the treatment intervention is estimated to have created. Rising medical costs and lowering QALY values in the review of a treatment plan's effects should not indicate for its continued use without very compelling justification of potential benefits. Noting the long-term cost burdens of cognitive decline shows how significantly this problem contributes to the excess of spending in healthcare.

Encouraging physicians to utilize Total Intravenous Anesthesia exclusively in cases where there is a higher propensity for the development of cognitive decline has the potential to reduce spending in the economy, but how should this be done? Due to the designed insurance structure, physicians are poorly incentivized to provide care at a low cost. However, the implementation of policies such as evidence-based care reimbursement programs that encompass the cognitive decline of patients in addition to the physical recovery from surgical intervention could promote a more economical and cost-conscious course of action. When there is little literature in support of inhalation anesthetics, the choice to use them should be an exception rather than practice for any surgical centers. The use of anesthetics that do not optimize outcomes not only costs patients more, but also increases Medicare spending. The time spent caring for the fallout of these complications also creates opportunity cost that is burdened by physicians

and families who help care for these patients. In a world where there is an increasing value placed on human capital, it is illogical to continue to minimize the risks of potential reductions in this resource. The consideration as well of patients with higher education being less at risk for POCD developing also means that these complications could disproportionately negatively impact low-income populations based on what is known about poverty's correlation with educational level attained. By taking more time in the preventative care aspect of surgery, there can be more done for these patients over the course of their life to improve their health and long-term wellness.

## CHAPTER 4

### Future Recommendations & Implications

In the final chapter, the lack of research relating patients with particular disease propensities and their response to general anesthetics will be highlighted and future actions for physicians, patients, and policymakers will be recommended. The conclusion will reinforce the findings of the cost analysis, advocate a treatment recommendation, and emphasize the importance of further research in the field being conducted to gather the necessary data. There will also be a discussion of how this research could impact the national percentage of spending for this sector to detail its importance to the wide-ranging economic climate.

Intravenous anesthetics demonstrate consistently lower rates of complication following surgery, including those involved with cognitive complications. Despite its initial start as a higher cost alternative to the traditional inhalation anesthetics, the developments in technology implemented in recent years allow for its cost to continue to decrease while maintaining the same benefits it has demonstrated in clinical setting. This is more likely to occur in intravenous anesthetics than in inhalation anesthetics due to inhalation anesthetics having a longer time period to become well established.

For patients with higher propensity for cognitive decline, this research suggests a further emphasis on educating them about their risks prior to surgical intervention. In light of the results discussed, clinical recommendations for care should consider the long-term implications of Post-Operative Cognitive Decline. POCD has been illustrated to

have high costs for patients in their recovery process. It should also be noted that the presence of cognitive impairments can further complicate the recovery for physical ailments. For example, a patient struggling to stay consistent in a treatment plan could improve their consistency through having improved short-term memory and ability to learn new information in cases of physical therapies or medication regimens. This level of preventative care could be difficult to incentivize physicians to comply with in a meaningful way. Patients could be incentivized to take part in preventative care through educational initiatives, since higher educational levels have shown to reduce prevalence and severity of cognitive decline. Educational intervention and cognitive training for recovery could also be helpful in treatment of Post-Operative Cognitive Dysfunction in cases where emergent surgery necessitates more invasive care that could lead to further cognitive decline. In order for cognitive ability to be of any concern to a patient, they must be able to maintain a degree of stability in their physical health. Surgical risks are rarely discussed in situation where consent is implied for patient care such as situations where a patient is unconscious or too sick to refuse care.

Research into the impact of different insurance incentives on the type of anesthetics used to illustrate the role that cost incentives play in physician decision making. The slight changes in outcomes on a long-term scale tend to be overlooked in the clinical setting for a combination of reasons. Hospital design and insurance market structures have long required an overhaul to reduce costs in the United States. One of the least controversial and more effective prescriptions for this market is preventative care. By further developing the longevity and wellness of patients, many of the more expensive



healthcare costs, can be avoided or minimized. This includes emergent hospital visits, unexpected surgeries, and clinical stays due to complications from coexisting conditions. In cases where surgical intervention is still required, taking care to minimize harm allows for more efficient recovery and is an important form of preventative care. The surgeon's responsibility to do no harm must encompass the weight of potential complications from anesthetics beyond those that may occur in the operating room. Clinical research investigating the impact of different anesthetics in specific surgeries and specific surgical populations is necessitated by the unforeseen consequences that anesthetics have on patients.

With this in mind, what insurance reforms have demonstrated evidence of success with similar types of problems in the healthcare markets? This section will examine the possibility of different healthcare policy initiatives for reductions in spending for anesthetics and incentivizing anesthesiologists to take part in using the lower cost, lower risk anesthetic. Prior in this thesis, the use of TIVA anesthetics over inhalation anesthetics was demonstrated to be consistently a lower-cost alternative with lower rates of POCD. The significance of POCD to the healthcare market spending was also illustrated as significant, emphasizing the demand for a lower cost alternative.

Healthcare policy initiatives that will be considered are bundled payment programs, Post-Acute Home Health, cost-sharing and incentive initiatives. The impact of competition in healthcare markets will also be discussed with mention to how this could impact the cost burden of these treatments and physician trends in decision making.

A variety of bundled payment programs have grown in popularity in recent years with varying levels of success. These programs can vary in the range of care that they cover but will typically provide a single payment for a comprehensive episode of patient care. This can include any and all services that are required underneath that time-frame of care or can be structured as inclusive to acute care only, acute and post-acute care, or post-acute care only. Bundled payment plan initiatives often also include financial and performance accountability since they frequently involve a variety of services. Medicare has exhibited more implementation of Condition Specific Bundled Payments (CSBPs) but commercial insurance markets have been slower to implement them. They have been praised for being a way to unite physicians and hospitals in providing high-quality, low-cost care for patients. This is illustrated in a study conducted by Whaley et. al in 2021, where an employer-provider direct payment plan was found to lead to a 10.7 percent relative reduction in cost of procedure (Whaley, 2017). This reduction was for commercially insured populations undergoing surgical care and all care in the 30 days following surgery, showing the success possible with these types of care models. There has also been some success of bundled payment plans in Medicare with the CJR model studies illustrating benefits from mandatory bundled care (Barnett et al., 2019). These studies note that the changes in spending are typically from reductions in post-acute care and some administrative costs while still maintaining positive patient outcomes. This would indicate that further experimenting with bundled payments could improve other surgical spending and incentivize physicians to use lower cost options for treatment that still have the same results associated.

This payment example could be an effective way to incentivize physicians to consider lowest cost anesthetics while still considering patient outcomes. In order to adjust this method to be applicable to POCD, I would recommend including a longer time period of recovery care for cognitive recovery services specifically. This could properly incentivize physicians and patients to take advantage of resources to fully recover cognitively from surgery in addition to physically. If the cost is already included within the bundled care model, they could be more likely to consider caring for this element of their health. This bundled payment model could also have anesthesiologists being involved in the negotiations for pricing of the service in order to emphasize their role in choosing low-cost options. The procedures that have exhibited the most frequent integration into these plans are orthopedic procedures, organ transplant surgeries, and other surgical interventions. With the similarities in some of the procedures it has demonstrated success for and some of the procedures in which Post-Operative Cognitive Dysfunction is most likely to develop, it could be a beneficial plan to implement some bundled payment initiatives to promote cost reduction.

Another potential method to reduce costs and improve recovery in patient models is to consider implementing Post-Acute Home Health. This method could also be combined with Bundled Payment Plans to further incentivize its use. This could be specifically beneficial for elderly patients in need of assistance to return to the level of autonomy they are accustomed to. In the case of cognitive decline, it can be crucial to have another individual present to recognize and track symptoms developing. Post-Acute home health is another example of a service that could be included under temporary

arrangements for the Bundled Care model, further incentivizing physicians to minimize unwanted cognitive impairments following surgery. The emergence of Post-Acute Home Health could be a way to more efficiently manage Post-Operative Cognitive Dysfunction or monitor for its emergence in the case of elderly patients with high likelihood of developing it because it is low cost and high autonomy, incentivizing patients to take an active part in their recovery. This lower cost alternative to lengthy hospital stays could allow for patient cognitive improvement to be more independent of nursing staff, promoting more intrinsic motivation for patients to proactively pursue this route of healing that requires active participation to demonstrate success.

A key concept in economics is the simple idea that incentives matter. In healthcare economics literature, research has consistently illustrated the crucial role of incentives in changing physician behavior. The healthcare market poses unique challenges to incentivizing physicians due to the structure of insurance markets and hospital billing. Incentives do not have to be effective at just motivating physicians to act in accordance, but also in incentivizing patients to complete treatment plans. In addition to this complication, policymakers have to make further considerations for challenges that are unique to the healthcare markets. A prime example of this is the prevalence of externalities in healthcare. In the case of cognitive decline following surgery, there is an externality created by the additional care and cost that these patients can incur. Presently, there is not enough research, education, or policies to protect against these externalities. As a result, they negatively impact parties who are not directly involved with the surgical procedure itself.

In addition to the concerns of externalities in healthcare markets, there is also the challenge of informational asymmetry in healthcare markets, particularly visible in cases like POCD following anesthesia. Informational asymmetry like the asymmetry found in healthcare prevents markets from functioning properly. Competition cannot be achieved if patients are not aware of the options they have for providers, care/services, or insurance policies and pricing. This is a major factor in the topics presented in this thesis. Most patients are not aware of the different options they have for anesthesia in surgery in addition to being unaware of the surgical risk of Post-Operative Cognitive Dysfunction. In addition, there are high opportunity costs for the research required to fully understand their options in a holistic way that enables them to make decisions about their care. This is a key reason why anesthesiologists must hold a greater respect for the responsibility they have for the market. When physicians are being placed into positions where they are highly trusted to make informed decisions for the consumer, it is imperative that they understand the ramifications of that.

There is also the concern of adverse selection, where individuals with higher risk of developing conditions tend to pursue insurance policies to minimize this risk more frequently than someone with lower risk. Adverse selection would demotivate policymakers from implementing things like the bundled payment care plans recommended for cognitive decline since the patients who are more likely to require those services are also the most likely to purchase from sellers with those features, further increasing the average risk in their risk pool. Moral hazard is an additional challenge for healthcare policymakers to consider in the solutions outlined here. This principle of

individuals tending to utilize more of a service because of a low level of cost-sharing in it could lead to overconsumption. For example, the moral hazard associated with a surgery is seen in patients electing to undergo unnecessary, expensive surgical trauma because it is covered in part or majority by their insurance. This can also lead patients to feel more comfortable with the insurance asymmetry present and lead to more complacent attitudes being developed with their lack of information. Some policymakers advocate for patients having more cost-sharing in the market to disincentivize the overconsumption of healthcare. This could be beneficial in preventing Post-Operative Cognitive Decline in case where the surgical intervention that led to its development was unnecessary and avoidable.

Healthcare competition must also be considered when evaluating best ways to reduce spending in the healthcare sector. The lack of true competition in markets is frequently cited as a primary reason for costs constantly rising beyond reasonable levels. In the case of POCD, the constraints placed on the market described above demonstrate how this can prevent patients from adequately shopping for the best option. Their cognitive outcomes from surgery are all too often not considered in the process of making a treatment plan for surgery or in creating a treatment plan for post-acute care or preventative care. However, this can be cited as more attributable to the informational asymmetry. If patients are not able to make decisions regarding their care due to a lack of information or power, how can this be alleviated. Educational initiatives for patients can be difficult to implement and measure compliance for in addition to the difficulties of incentivizing their use in practical ways. With this in mind, a more logical option

could be to further educate physicians on basic healthcare economics to promote more cost-conscious behavior. In the case of anesthetics, ensuring that anesthesiologists are aware of the opportunity costs of each option and the significance behind this could allow for an uptick in cost-minimizing behavior.

Hospital mergers are on the rise as the market is consolidated at staggering rates. Advocates for these shifts in market structure claim that they boost coordination of care, leading to more value-based outcomes. For anesthesiologists, this could mean a more standardized practice of treatment for patients and reduction in costs of the associated anesthetics. However, the literature surrounding these market consolidations has a much gloomier outlook. In the case of a study published by Eliason et al in 2020, patients on dialysis care that were involved in a hospital merger saw significantly decreased patient outcomes and increased drug reimbursements (Eliason et al, 2020). This echoes the outcome cited by other recent literature and raises the question of to what degree hospital mergers will continue to skyrocket costs. This example is similar to the plights of POCD concerns in anesthetic use because of the nature of the market for each treatment. Similar to dialysis, surgical patients do not frequently shop different anesthesiologists or anesthetic methods, demonstrating that principles of market power should align between the two. Another concern that hospital mergers create with this data is that of increased drug use for patients underneath a new structure where there is less concern that insurance will reject billing of treatments deemed unnecessary. Repeated and prolonged or excess exposure to anesthetics is one of the main risk factors for developing Post-Operative Cognitive Dysfunction, making this particularly concerning. If hospital

mergers are to truly cut down costs and increase efficiency, then patient outcomes must be considered at the forefront.

This research was limited by access to data on healthcare outcomes being restricted due to privacy law and ethical concerns. This research is also limited by the simple fact of it being improbable and impossible for anesthesiologists to be blinded to patient pools prior to treatment being administered, limiting the possibility for any sort of Randomized Control Trail to take place. It is also unethical to conduct an RCT for patients with varying levels of cognitive functioning by assigning them to surgical or non-surgical groups or even intravenous/inhalation anesthetic groups. Further, there is the concern of Post-Operative Cognitive Dysfunction being a condition that requires formal cognitive testing prior and post-surgery to be detectable beyond self-report, something that seldom happens outside the research setting. There is additionally the complication of surgical patients likely having distinct differences from non-surgical patients, causing there to be a weak level of identification assumption in an empirical study. To overcome these concerns requires high levels of controls in data to minimize bias.

While this type of testing may be costly to implement, this research demonstrates the importance of care that considers this element. Further, many of these studies have underrepresentation of those with lower education, minority groups, those with language barriers, etc. which complicates generalizability. As mentioned earlier, POCD is not a condition that is an exception to the growing understanding of low-income populations being disproportionately affected by poor healthcare policy. There is also the limiting



factor of testing for cognitive outcomes being conducted with a variable frequency at variable time intervals across studies. It is also imperative to note the potential complication of patients recovering from surgery likely being administered medications that alter cognitive functioning to a degree. This additional factor complicates the decision of when patients should be tested for the most accurate measure of neurocognitive recovery in hospital setting. This is especially evident in patients with propensity for these diseases and cases where high cognitive functioning is of primary concern for the patient. Despite all of these challenges, considering this data provides strong evidence for the existence, significance, and preventability of POCD through care in selecting an anesthetic method. This research should encourage policymakers to continue to attempt to minimize costs while maintaining patient outcomes and accessibility in addition to promoting continued research in the field. The costs associated with POCD in addition to the suggested policy changes should incentivize anesthesiologists to have a greater awareness and respect for their responsibility in the market. The role of a physician must go beyond the hospital setting to truly select a treatment plan with the highest utility for their patients.

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