Evaluation of a COVID-19 Surgical Scheduling Guideline using the Appraisal of Guidelines for Research and Evaluation AGREE II Instrument

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ABSTRACT

Introduction/Background: Since the beginning of the SARS-COVID-19 pandemic in February 2020, the operating room and surgical care has undergone vast change. At its start, COVID-19 infection caused many elective surgeries to be canceled, operating room schedules to be altered, and inquiries of how healthcare should change in order to continue providing the best care during unprecedented circumstances. Hospital administration, healthcare workers, and patients began searching for valid information to guide best practice. COVID-19 has been found to severely affect the physiology of the circulatory and pulmonary systems of patients. With new discovery of pathophysiologic consequences of COVID-19 infection, the need for well-founded guidelines to assist clinicians in managing surgical and anesthetic care is realized. Guidelines surrounding the treatment of surgical patients infected with COVID-19 were formed during a time of crisis when evidence was limited and instability in healthcare delivery occupied much of healthcare team efforts. This period of uncertainty, paired with the volume of patients infected with COVID-19, may have contributed to the development of unclear guidelines as well as inconsistencies in following established guidelines that were meant to direct surgical and anesthesia care during times of peak infection of the COVID-19 pandemic.

Method: The main purpose of this Doctor of Nursing Practice (DNP) final project was to evaluate a clinical practice guideline (CPG) designed to be used by anesthesia providers to guide timing of surgery for patients diagnosed with COVID-19 in a major midwestern hospital in Michigan. The surgical scheduling guideline was evaluated for overall quality, development, and reporting using the AGREE II instrument and following instructions from AGREE Enterprise. The quality improvement methodology for this project followed the Agency for Healthcare Research and Quality's "Plan-Do-Study-Act'' model for testing an implemented change. The

appraisal team consisted of four appraisers that examined the CPG guideline. All items within the AGREE II instrument were given a score on a Likert scale ranging between 1-7 (strongly disagree = 1 and strongly agree = 7). Quality scores corresponding to six domains of the AGREE II instrument were calculated in addition to a compilation of the overall quality of guideline scores.

Results: The guideline received low appraisal scores for the domain categories contained in the AGREE II instrument. All quality scores for the six appraised domains were low except for Domain 4: Clarity of Presentation (65.28%). In addition, the guideline received an overall low guideline quality rating of 25%. Although all domain scores and the final appraisal score were low, three out of four appraisers would recommend the guideline for use with modifications.

Discussion: Large contributors of poor appraisal scores **were** the lack of available supporting evidence and explicit language needed for continual use and improvement. In developing future practice guidelines that will assist in upholding the delivery of safe surgical and anesthesia care even during an unprecedented crisis such as the COVID-19 pandemic, it is essential to include source materials to lend transparency for clinician use. Additionally, guidelines intended to influence patient care outcomes should include explicit evidence and language that states the desired outcomes. Additions such as these would better ensure the assessed guideline would contribute to positive change in patient care.

Keywords: COVID-19, guidelines, Agree II Instrument, anesthesia, surgery

TABLE OF CONTENTS

LIST OF SYMBOLS & ABBREVIATIONS

Surgical Scheduling Considerations After COVID-19 (SSCAC)

Corewell Health East-William Beaumont University Hospital (CHE-WBUH)

DVT: Deep Vein Thrombosis

PE: Pulmonary Embolism

CVA: Cerebral Vascular Accident

AKI: Acute Kidney Injury

MI: Myocardial Infarction

AGREE II: Appraisal of Guidelines for Research and Evaluation II

PDSA: Plan-Do-Study-Act

CMR: Cardiac Magnetic Resonance imaging

CPG: Clinical Practice Guideline

DNP: Doctor of Nursing Practice

CRNA: Certified Registered Nurse Anesthetist

SRNA: Student Registered Nurse Anesthetist

LIST OF APPENDICES

Evaluation of COVID-19 Surgical Scheduling Considerations using the Appraisal of Guidelines for Research and Evaluation II Instrument

Since the beginning of the SARS-COVID-19 pandemic in February 2020, vast changes in the management of surgical and anesthesia care have taken place. COVID-19 infection caused many elective surgeries to be canceled and operating room schedules to be altered, especially at the start of the pandemic. Using predictive modeling, the United Kingdom's National Institute for Health and Care Research (NICR) estimated that 28,404,603 surgeries were postponed or canceled globally in the peak 12 weeks of disruption during the initial COVID-19 pandemic outbreak (COVIDSurgCollaborative, 2020). Complications related to postponement of this magnitude affect national health care and the financial implications of surgery postponement are unprecedented.

With such disruptive circumstances presented to surgical and anesthesia care, many hospital administrators and health care providers questioned the care provided and sought out best practice, valid information, and guidance on how to continue to provide the safest care for patients. Organizations such as the NICR advised the development of plans and strategies to recover from these necessary pauses in surgical scheduling in a safe way (COVIDSurg Collaborative, 2020). The desire to mitigate risk and promote health through maintenance of evidence-based anesthesia and surgical practice is imperative for providing safe patient outcomes, especially amidst continued COVID-19 infection. Planning for future protection against pandemic scale events is vital in ensuring betterment of our healthcare system and emergency preparedness.

The primary target of COVID-19 virus is the pulmonary system; however, the virus is also known to cause endothelial dysfunction, vascular inflammation, and alterations in the

coagulation cascade. Together these changes contribute to higher rates of deep vein thrombosis (DVT), pulmonary embolus (PE), and cerebrovascular accident (CVA) (Bryant et al., 2022). In addition, pulmonary complications, myocardial injury (MI), and acute kidney injury (AKI) are thought to result from regional inflammation and cytokine release as a consequence of COVID-19 infection (Nadim et al, 2020).

A study by the American College of Cardiology found that pulmonary edema secondary to viral myocarditis was found to be present in a significant number of otherwise healthy subjects after SARS-CoV-2 infection (Huang et al, 2020). The potential for COVID-19 to alter myocardial conduction, strength, and valvular function has significant implications to anesthesia care (Sattar, et al., 2020). Effective alveolar gas exchange has been shown to affect two major functional components: the integrity of alveolar epithelium and the patency and function of alveolar microcirculation. The inflammatory process that results from the infection activates the direct contact pathway for thrombosis formation (Wang et al., 2020). This presents the threat of venous thromboembolism and resultant pulmonary emboli.

The sequelae of COVID-19 portrays the increased mortality risk for surgical patients. Further, research has shown that undergoing anesthesia prematurely after recovery from COVID may increase the risk of postoperative complications and mortality (Deng et al., 2022). An international cohort study by the Lancet in 2020 suggests, "...consideration should be given for postponing non-urgent procedures and promoting non-operative treatment to delay or avoid the need for surgery" (Nepogodiev et. al, 2020). Furthermore, the NIHR wrote, "Patients infected with COVID-19 scheduled for surgery within 6 weeks of infection are at an increased risk for morbidity and mortality (COVIDSurg Collaborative; GlobalSurg Collaborative, 2021). It is clear that timing of surgery and pathology are linked to patient outcomes.

The Anesthesia Patient Safety Foundation (2021) submits that establishing the optimal timing of procedures for patients who have recovered from COVID-19 infection and the appropriate level of preoperative evaluation are challenging due to the lack of current evidence on the specific issue of surgical timing. Corewell Health William Beaumont University Hospital (CHE-WBUH) developed scheduling guidelines that indicate when patients should be scheduled for surgery after testing positive for the COVID-19 virus (Appendix A). The guideline titled, Surgical Scheduling Considerations After COVID-19 (SSCAC) includes information on infectivity, considerations for post COVID-19 timing of surgery, and consideration of patient vaccination status (Appendix A). Corewell Health East established use of SSCAC to limit exposure to staff and mitigate the risk of postoperative complications. These guidelines were set in place early on in the pandemic with no precise installation date on record.

The CHE-WBUH Surgical Scheduling Considerations After COVID-19 guideline has been in place for over two years and was developed at a time when little information was available to direct development of such a tool. Given the current knowledge and implications associated with COVID-19 infection, the guideline may not be based on the most valid evidence to dictate surgical and anesthesia care. Although multiple studies have examined the overall risk of mortality after COVID-19, the relationship between surgical timing and COVID-19 infection with regards to patient morbidity and mortality warrants further investigation. Further, while the COVID-19 pandemic has transitioned to an epidemic, the need for a strong guideline is crucial to ensure confidence in protecting future patient outcomes.

AGREE II Instrument

The Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument was identified as the best method for guideline examination as it is considered the gold standard

appraisal instrument exclusively designed for clinical guidance documents (O'Shaughnessy, et al., 2022). AGREE II has been validated across multiple specialties and applies a series of 23 items which propose questions used to interrogate clinical guidelines for quality and integrity. The instrument was developed to address clinical practice guideline variability and quality by assessing the methodological rigor and transparency during development (AGREE Project, 2009). The instrument provides a framework to assess the quality of guidelines, provide a methodological strategy for the development of guidelines, and informs what information and how information ought to be reported (AGREE Project, 2009). The instrument is intended to be used by various stakeholders, including: healthcare providers, guideline developers, policy makers, and educators. Education regarding the AGREE II instrument is freely available through AGREE Enterprise website, allowing any stakeholder the ability to utilize the instrument.

Literature Review

Literature Review Method

In preparing to perform a guideline appraisal, the authors performed a literature review on the sequelae of COVID-19 infection which would offer the most thorough starting point of investigation. The following literature review revealed how the sequelae of COVID-19 poses a risk for increased mortality of surgical patients and significant implications in anesthesia and surgical care. Knowing this, a literature review that supports evidence based guideline development for guiding decision making of surgical timing after COVID-19 infection was essential.

A literature review pertaining to the pathophysiologic effects of COVID infection was performed using the following databases: CINAHL complete (Cumulative Index to Nursing and Allied Health Literature) through EBSCO host, Cochrane Library, PubMed, and Google Scholar.

Given that COVID-19 is a recent occurrence, only relevant articles published between November 2020 and December 2022 were included. Keyword search terms included: “COVID-19”, “coronavirus”, “long term”, “respiratory”, “pulmonary”, “lungs”, “myocarditis”, “cardiomyopathy”, “surgery”, “anesthesia”, “arrhythmia”, and “adverse events”. Keyword search included “anesthesia AND COVID-19 OR coronavirus”, “COVID-19 OR coronavirus AND surgery AND outcomes”, “COVID-19 AND cardiomyopathy”, COVID-19 AND respiratory” “surgery”, “postoperative complications”, and “adverse events”.

Respiratory Sequelae

When examining the effects of COVID-19, the profound pathologic respiratory complications are cited most frequently. Supplemental oxygen dependency, increased ventilatory requirements, compounded by hospital shortages of ventilators, ICU rooms and hospital staff are common concerns among the public due to COVID-19’s profound impact on the respiratory system. Respiratory complication research, exploring the long term respiratory effects of the virus, is still emerging. At this point, COVID-19 respiratory sequelae is related to previous SARS infections: the virus causes intra-alveolar thrombosis and viral inflammatory damage to the airways which contributes to development of fibrotic changes in the pulmonary system (Wang, et al., 2020).

One of the newly discovered methods of COVID-19 access to the intracellular systems of the body is via the angiotensin-converting enzyme 2 (ACE2) receptor on relevant cell surfaces. “Many factors have been associated with both altered ACE2 expression and COVID-19 severity and progression, including age, sex, ethnicity, medication, and several co-morbidities, such as cardiovascular disease and metabolic syndrome” (Bourgonje, et al., 2020). These receptors are highly prevalent in pulmonary tissues. This is where the body converts angiotensin I to

angiotensin II in the Renin-Angiotensin system and where the ACE2 receptor is known to regulate other byproducts of the conversion including variables of bradykinin and ghrelin. It is the proliferation of these receptors, not necessarily their function, which is exploited by the COVID-19 virus. The virus structure has an affinity for the receptor which leads to proliferation in a multitude of body tissues (Shang, et al., 2020). Bourgonje et al. (2020), explain: "ACE2 [is] highly expressed on lung alveolar epithelial cells and small intestinal epithelial cells, consistent with potential routes of viral transmission of [COVID-19]. [ACE2] is present on vascular endothelial cells and smooth muscle cells in all organs studied … ACE2-expressing organs do not equally participate in COVID-19 pathophysiology, implying that other mechanisms are involved in orchestrating cellular infection resulting in tissue damage".

Within the pulmonary tissues, COVID-19 has also been found to directly attack type 2 pneumocytes by binding to the cell surface and destroying the cells through viral multiplication and reproduction (Wang, et al., 2020). The combination of these two proliferation methods causes profound damage within the pulmonary tissues, which are now being attributed to longer-lasting sequelae.

A relationship between the severity of the viral infection and severity of lung damage has been established (Wang, et al., 2020). According to Wang et al., "The virus can injure the lungs in three ways: acute respiratory distress syndrome (ARDS) with diffuse alveolar damage (DAD), diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation. The results of these combined actions include impaired alveolar oxygenation, hypoxemia, and acidosis." These processes lead to extensive diffuse alveolar damage with bilateral edema, alveolar exudates, and diffuse reactive hyperplasia of type II pneumocytes which is consistent with fibrosis (Bourgonje et al., 2020). In essence, pulmonary

changes resulting from COVID-19 infection may initially present as pneumonia but the acute lung damage may result in chronic impairment of fundamental lung physiology which can result in impaired quality of life. Given these substantial physiologic changes brought on by COVID-19 the possibility of unforeseen complications in surgical patients who undergo anesthesia.

COVID-19 Associated Myocarditis

An article written by Hirata & Yamakage (2020) titled, *Cardiovascular Considerations for Anesthesiologists During the COVID-19 Pandemic,* multiple avenues of COVID-19 specific cardiac complications with anesthesia specific implications are discussed. The authors gathered emerging data to highlight important perioperative cardiovascular considerations associated with COVID-19 infection. They found a high incidence of myocardial injury and cardiomyopathy in patients with severe COVID-19 between 7.2-27.8%. These injuries and abnormalities range from left ventricular dysfunction, persistent hypotension, myopericarditis, myocarditis, arrhythmia, and heart failure. They suggested several mechanisms of cardiac injury such as direct viral invasion, systemic inflammatory responses, coagulation disruptions, and pneumonia induced hypoxia as contributing or causative factors. A parallel between severe sepsis induced myocardial complications caused by excessive inflammatory response and COVID-19 infection was drawn, citing the elevation of proinflammatory cytokines, and hypercoagulable state with both disease processes. A suggested mechanism of COVID-19 cardiac and pulmonary cell infection by way of ACE2 receptor infiltration was proposed based on ongoing research, attributing myocardial and lung injury to direct viral infiltration within the cell (Cohen et al., 2020). Anesthetic concerns include exacerbated inflammatory responses during surgery and intensified cardiovascular disease processes which increase morbidity and mortality with increased cardiac risk factors such as hypertension, diabetes, hyperlipidemia, atherosclerosis, and

advanced age. Finally, the authors propose that vigilant monitoring of cardiac status is warranted with COVID-19 patients due to their increased cardiac risk status. Further research needed to improve perioperative management of COVID-19 patients (Hirata & Yamakage, 2020).

Given the ACE2 receptor theory of cardiac tissue infiltration of the COVID-19 virus, several studies have found myocarditis to be prevalent among those who have had a COVID-19 infection. A study performed by Huang, et al (2020) found evidence of persistent cardiac disease in patients recovered from COVID-19 after evaluation using cardiac magnetic resonance imaging (CMR). A single center retrospective observational study of 26 patients who reported cardiac symptoms after acute recovery from COVID-19 was also acquired by this literature review. Importantly, these patients did not have baseline studies performed prior to COVID-19 infection. Of the 26 patients, 15 were found to have abnormal CMR findings including myocardial edema in 14 patients, and 8 who presented with late gadolinium enhancement- a finding associated with prediction of adverse cardiovascular outcomes in patients with nonischemic cardiomyopathy. Patients were also found to have decreased right ventricular function. The researchers conclude that because traditional acute viral myocarditis does not include these abnormal CMR findings, the existence of diffuse myocardial edema and fibrosis is specific to COVID-19 infection. The major weakness of this study centers around the small sample size and a non-random sampling of patients. Additionally, the majority of patients exhibiting moderate COVID-19 infections may be non-reflective of severe and critical infections. The study demonstrates the phenomenon of cardiac involvement post-COVID-19 which can be used to inspire further necessary research (Huang, et al., 2020). However, the researchers admit results cannot be extrapolated to a larger population.

A systematic review of abnormal cardiovascular magnetic resonance findings in recovered COVID-19 patients was performed by Kim, Han & Suh (2021). This review included 890 patients from 16 studies. All CMR scans were performed within 22 weeks of COVID-19 recovery. The researchers found abnormal CMR findings in recovered COVID-19 patients to be 46.4%, with explicit myocarditis and late gadolinium enhancement in 14% and 20.5% of cases respectively. With retrospective analysis, the researchers gathered that patients with normal cardiac enzyme levels and athletes had a lower prevalence of abnormal CMR findings. The researchers cited various limitations of small sample and subgroup sizes, lack of robust subgroup analysis, and limited analysis of ventricular systolic dysfunction. The lack of robust subgroup analysis was attributed to a lack of data such as presence of specific cardiac symptoms, underlying cardiac disease, and ECG or echo abnormalities. Similar to other evidence based studies explained thus far, Kim, Han, & Suh describe a need for longer-term studies to determine clinical significance of these findings.

COVID-19 Induced Arrhythmia

A systematic review and meta-analysis by Garcia-Semora et al (2020) estimated the presence of ECG abnormality and cardiac arrhythmia in hospitalized patients with COVID-19 infection. Additionally, association of arrhythmia with patient outcomes were made. Analysis of the 30 included studies show that supraventricular tachycardias, ventricular tachycardias, QT prolongation, ST segment deviation were the most common arrhythmias present in patients with COVID-19 infection. Associated outcomes included mechanical ventilation, development of further arrhythmia, worse prognosis, and increased mortality. Limitations to this study were an under reporting of arrhythmia type in half of the included studies which limited practical application to clinical care provided. Additionally, the review did not include assessment of

long-term outcomes of COVID survivors which makes a direct connection to subsequent anesthesia-based research less likely. However, being the largest meta-analysis surveying ECG changes in COVID-19 patients provided a valuable starting point for future inquiry.

A review paper by the American Journal of Medicine pertains directly to the newly observed phenomenon of cardiac arrhythmia present during Post-Covid Syndrome. Stalberg et al., (2021) write, "Given the extremely high number of reported cases and the uncertain long-term prognosis, post-acute COVID-19 syndrome is likely to become a major clinical problem for the foreseeable future." They note increased frequency of abnormal sinus tachycardia and premature ventricular contractions among COVID-19 survivors and consider a post-covid tachycardia syndrome presents as a subsyndrome of post-acute COVID-19. While the paper does not include statistical backing of its claims, it does provide another foundation for further research relating to anesthesia care. Treating post COVID-19 arrhythmias as a novel clinical syndrome, performing interventional studies and testing established pharmacological interventions against the novel syndrome again highlights the purpose of subsequent research.

Another review article by Sattar et al (2021) provides a concise description of the pathophysiology and treatment of the cardiac sequelae of COVID-19 infection. The impact of COVID-19 on the cardiovascular system is summarized as evidenced by multiple studies. They report myocarditis in 7–17%, heart failure in 24%, arrhythmias in 17% and thrombotic complications in 31% of hospitalized COVID-19 cases. The review is again limited by lack of statistical method to demonstrate significance and effect; however, it remains useful in demonstrating the need for prevention and treatment of cardiac sequelae to limit morbidity and mortality for our patients (Sattar et al., 2020).

Neurological Sequelae

COVID-19 has shown to invade almost every tissue within the body and brain tissue is no exception. “Increasing reports have shown that [COVID-19] infection involves the central nervous system and the peripheral nervous system and directly or indirectly damages neurons, leading to long-term neurological sequelae” (Wang, et al., 2020). Sattar et al describe how ‘Covid Long-Hauler’ syndrome presents as prolonged brain fog and difficulties with cognition (2020). Cognitive presentations such as anxiety, depression, insomnia, memory loss and cognitive changes have been previously described one year after covid infection (Han, et al., 2022). In a qualitative study of covid patients one year after infection, some degree of motor impairment has been observed in approximately 25.8% of subjects (Bellan, et al., 2022).

Wang, et al., (2020) summarize the physiology of COVID-19’s invasion into neuronal tissues in three distinct ways. First, the widely established ACE2 receptor is widely expressed in brain vascular endothelial cells, allowing COVID-19 access to cells which control the brain’s blood supply. Second, the invading S protein of the COVID-19 virus can directly damage the integrity of the blood brain barrier to varying degrees. Third, the virus can induce the inflammatory response of the microvascular endothelial cells that change the function of the blood brain barrier. As previous studies have mentioned, neurological symptoms as described as “Covid Long-Hauler syndrome” , cognitive impairment and memory loss are prevalent among recovered COVID-19 patients. The physiology of COVID-19 invasion into neuronal tissue is widely described and cannot be ignored.

Thromboembolic Events

A current topic among news headlines is the occurrence of blood clots in patients who have been infected with COVID-19 as well as among individuals who have received the vaccine.

Current literature does not have a clear consensus on the long-term thrombotic sequelae of previous COVID-19 infection though evidence of hematologic and inflammatory response has been noted in literature. COVID-19 infection contributes to patient risk by the infection triggering release of cytokines and rampant bradykinin. Bourgonje et al write, “patients are at particular risk for developing coagulopathy reminiscent of disseminated intravascular coagulation (DIC) which was associated with mortality, possibly due to both venous and arterial thrombosis” (2020). The authors continue with description of COVID-19 virus affinity and prevalence of ACE2 receptors as well as the role COVID-19 has in increasing susceptibility to blood clot formation through interactions and effects with bradykinin, endothelial mediators and biomarkers of endothelial activation (Bourgonje, et al., 2020). A paucity of research on the pathophysiologic effects of COVID-19 infection and implications for surgical and anesthetic research is a common theme from this literature review, and hematologic implications follow this need for further study.

Scheduling of Surgery After COVID-19

An emerging area of study is the timing of surgery in relation to a patient’s COVID-19 infection. Vranis et al (2021) note that it is imperative for health care providers to clearly convey the risks associated with each procedure while also acknowledging how other factors such as COVID-19 infection may also alter the patient's risk profile. In a study by the British Journal of Surgery in 2020, authors identified that more research is needed to verify guidelines that will offer clinical benefit and the optimal length of time for delaying surgery in patients with COVID-19 infection.

A study published in the journal “*Annals of Surgery*” (2020) helps to stratify the timing of infection in relation to postoperative complications. Authors conclude that major elective

surgery scheduled 0 to 4 weeks after COVID-19 infection is associated with an increased risk of postoperative complications. Surgery performed 4 to 8 weeks after COVID-19 infection is still associated with an increased risk of postoperative pneumonia, whereas surgery scheduled 8 weeks after COVID-19 diagnosis is not associated with increased complications. The American Society of Anesthesiologists and the Anesthesia Patient Safety Foundation (2021) have recently published updated guidelines advocating for waiting ≥ 7 weeks to schedule elective surgery for unvaccinated patients and to weigh the risks of the procedure against time sensitive needs in all patients. A multi-country study (116) and multi-center study (COVIDSurg Collaborative, 2021) followed more than 140,000 patients with 3127 having a COVID-19 infection demonstrating a 30 day mortality of 3.09 (CI 1.64-4.54) for patients having surgery 0-2 weeks following infection and a continual decline in risk to 0.64 (CI 0.20 – 1.07) ≥ 7 weeks following infection. The risk for patients without a COVID-19 infection was similar to waiting ≥ 7 weeks and was 0.62 (CI 0.57-0.67). This evidence highlights the implications of how scheduling of surgery contributes to patient risk.

Conclusion

After an extensive review of the literature pertaining to the complexities surrounding the sequelae of COVID-19 on survivors, several conclusions and limitations were established. One aspect is clear: data and information related to this issue is still developing. Further, the volume of cases related to the desired research area with adequate follow up for long term study is low, hindering the ability to identify distinct practice guidelines at this time. This review of the literature supports a quality improvement initiative to assess the quality and validity of surgical scheduling guidelines that contribute to outcomes of surgical patients who are post COVID 19 infection and scheduled for surgery.

Problem Statement

The following PICO question is proposed: In patients receiving surgical care at CHE-WBUH (P) how does the SSCAC score (O) when appraised using the AGREE II instrument (I)? The primary outcome of this project is to obtain an overall guideline assessment score for the CHE-WBUH SSCAC guideline. The secondary outcomes are to render individual AGREE II ratings for each domain in the appraisal tool (Domain 1–6). Using the AGREE II instrument the project members will evaluate the quality of the SSCACC as a clinical practice guideline for use in CHE-WBUH surgical and anesthesia care. Additionally, this project team hopes to gain insight on the methodological strategy for guideline development as well as how information should be reported in clinical practice guidelines.

Framework

This quality improvement project will utilize the framework developed by late physician and public health researcher and professor, Dr. Avedis Donabedian. Donabedian's framework for quality improvement was developed through his extensive research and career dedicated to theory and practice of quality assurance at both the Harvard School of Public Health and the University of Michigan. Since 1966, his developed framework has been utilized for the evaluation and assurance of quality patient care. His work has been highly referenced in many quality endeavors from trauma healthcare settings to emergency department COVID-19 response (Ayanian & Markel, 2016).

The framework itself consists of three parts that work synergistically in relation to quality improvement (Appendix I). These parts are: Structure, process, and outcome. Structure refers to the characteristics of the health care setting where patient care occurs such as equipment involved in patient care and the physical building where care takes place. Characteristics of the

process aspect of Donobedian's model include examples such as the delivery of care to patients and the workflows involved in doing so. Lastly, characteristics of the outcome aspect of the model describe the effects of health care on populations. Moore et al (2015) summarize the synergy between the three parts of the model with, "...according to this model, improvements in the structure of care should lead to improvements in clinical processes, which should in turn improve patient outcome." The simple design of the model lends itself as a concise foundation for complex quality improvement efforts that are associated with COVID-19 to materialize from.

Further explanation of the theoretical framework is provided by an article written by Donabedian himself. He emphasizes how a distinction between values and elements of a structure and outcome should be separately recognized, maintained, and equally studied in order to provide meaningful and lasting quality assurance in healthcare (Ayanian & Markel, 2016). With this in mind, the authors note that Donabedian's model offers an excellent opportunity for a simple and focused theory to base the project's theoretical framework. Additionally, the framework will provide study design for assessment of multiple yet likely connected variables pertaining to COVID-19 infection as they relate to evidence based guideline development and validity. The COVID-19 pandemic and the resulting effects on healthcare have become immensely complex. Therefore, quality improvement efforts must yield high scores when appraised in order to maintain integrity of positive patient outcomes despite trying conditions present in healthcare delivery.

After conceptual review of the components of the Donabedian framework, the project theoretical framework is easily applied to this quality improvement project. Structural components of this project include the setting of Corewell Beaumont East. Additionally, the

equipment involved with project implementation include the AGREE II instrument and the SSCAC which are classified as structural components in the Donebedian model.

Process components include preoperative scheduling of surgical care, COVID-19 preoperative testing, COVID-19 testing criteria, notification and communication regarding patient care among staff, throughput of surgical care into the post anesthesia care unit and discharge of patients from CHE-WBUH. Outcome characteristics for this review include the development of valid guidelines pertaining to the scheduling of surgery after COVID-19 infection and reduction in negative postoperative patient outcomes such as arrhythmia, increased oxygen requirements, and increased morbidity and mortality. By applying Donabedian's established and concise framework to this study design, the authors strive to bring attention to the importance and need for guidelines that are evidence based, valid, and offer transparency to patients and clinicians regarding surgery after COVID-19 infection and postoperative outcomes.

Project Methodology

This project utilized the Agency for Healthcare and Research (2020) Plan-Do-Study-Act (PDSA) methodology (Appendix H). The cyclical nature of the PDSA method of quality improvement method lends continual maintenance for guideline development and improvement. This is especially relevant in ensuring quality, validity, and integrity of the SSCAC guidelines. Additionally, the method allows the project to continue evolving into future quality improvement initiatives. Whether continuation of this quality improvement is by nurse anesthesia students or other clinicians, the PDSA model provides a simple foundation for continued access of work related to surgical patient outcomes after COVID-19 infection.

The project method included planning to appraise the SSCAC guidelines, appraising the guidelines, studying the results and scores of guidelines appraisal, and making recommendations

based on the obtained scores of appraisal. Future projects can expand on this project's initial PDSA cycle by incorporating guideline editing and performing research of COVID-19 patient outcomes through retrospective chart review and data collection. The PDSA method provided the project team with clear answers on what was to be accomplished: obtaining appraisal scores using AGREE II for the SSCAC. The PDSA model also allowed the project team to understand how change in the SSCAC guidelines could be identified as an improvement and how to set intentions for what changes should be made in the SSCAC to result in this improvement.

Project Design

The AGREE II instrument was the keystone of this quality improvement project. The project design follows the published instructions from AGREE Enterprise. AGREE Enterprise directs that a minimum of two appraisers implement guideline appraisal with four being preferred to increase reliability (Brouwers et al., 2010). Therefore, the four appraisers of this quality review were: Dr. Lori Shannon, DNAP, CRNA, Dr. Anne Hranchook, DNP, CRNA, Carolyn Olmsted BSN, RN, SRNA and John Hintzman BSN, RN, SRNA. Appraisers met in person to perform the appraisal and to reach consensus on how certain domains should be scored using the AGREE II instrument. Each appraiser scored 23 separate items for evaluation using the specific directions and considerations highlighted in the AGREE II User Manual (Appendix B) for clear interpretation of each item. Appraisers scored all items using a seven point Likert scale that corresponded with statements ranging from strongly disagree (1) to strongly agree (7). Items were categorized into six domains which organize appraisal items into the following categories: Scope and Purpose, Stakeholder Involvement, Rigour of Development, Clarity of Presentation, Applicability, and Editorial Independence. Following appraisal of the 23 items by each of the four appraisers, quality scores were calculated for each of the AGREE II domains. Domain

scores were converted into a percentage to represent a quality rating.

Findings of this quality improvement appraisal were presented at the Oakland University-Beaumont DNP-NA Dissemination Day on June 9th 2023. The presentation included a verbal overview, visual aids (PowerPoint), and an interactive discussion.

Project Setting

This project setting was CHE-WBUH, a midwestern hospital located in Michigan.

Key Personnel/Stakeholders

The key stakeholders for this project include:

1. CHE-WBUH Surgical patients
2. CHE-WBUH Director of Epidemiology
3. CHE-WBUH Senior Director of Surgical Services
4. CHE-WBUH Surgeons
5. CHE-WBUH Anesthesiologists & Nurse Anesthetists
6. CHE-WBUH nurses and healthcare staff of the interdisciplinary surgical and anesthesia teams

Participants

This DNP project included four team members in the appraisal process, as recommended in the AGREE II user manual. Two of the participants were experienced Certified Nurse Anesthetists (CRNAs) who were knowledgeable of Corewell Health surgical scheduling practices and two were student registered nurse anesthetists (SRNAs) who were in training at the facility.

Results

The AGREE II instrument involves 2 or more researchers, identified by the tool as (healthcare instructors, RNs, learners, etc.). The researchers are then asked to evaluate the

clinical practice guideline in 23 separate items separated into 6 Domains with an additional final recommendation at the end. Each domain was scored on a Likert scale from 1 - 7 with 7 being the highest and 1 being lowest possible score. The scores are then aggregated as described within the AGREE II tool, which yields a percentage from 0% to 100%, with 100% being the highest possible score.

The first domain entitled 'Scope and Purpose' contains three items relating to the 1) Objectives of the guideline, the 2) Questions covered by the guideline, and the 3) Population for which the guideline was written to apply. Reporting criteria for the objectives of the guideline include the health intents of the guideline. I.e., interventional, preventive, diagnosis, or treatment, the expected benefits/outcomes of the guideline, and the target population for which the guideline is intended to help. Reporting criteria for the questions asked by the guideline included the targeted population, interventions or exposures, comparisons to other guidelines, outcomes to be achieved and health care settings/context within which the guideline is set. Reporting criteria for the population of the guideline includes the target population sex and age, clinical condition, severity/stage of disease and comorbidities included within the guideline, as well as excluded populations. Domain 1 'Scope and Purpose' was scored at 4.17% by the appraisers.

The second domain entitled 'stakeholder involvement' contains three items relating to the 1) Group Membership of the individuals responsible for development of the guideline, 2) Target Population preferences and views of the guideline by which populations the guideline is intended to cover, and 3) Target users of the guideline. Considerations for scoring in these items were topics such as the name, discipline, and professional relationships of the writers, intended

audience for use, and a statement of acknowledgement for the preferences of the target population. Domain 2 ‘Stakeholder Involvement’ scored 5.56%.

The third domain entitled ‘Rigor of Development’ is evaluated by 8 items including 1) Search Methods for the reporting of the evidence used during development, 2) Evidence selection criteria with rationale for selection, 3) Strengths and Limitations of the evidence provided with rationale, 4) Formulation of Recommendations which covers how the recommendations encompassed within the guideline were made in regard to the presented evidence, 5) Consideration of benefits and harms which evaluates the risks , health benefits, and side effects that were considered when formulating recommendations, 6) Link Between Recommendations and Evidence which is the explicit link between the evidence found and the recommendations made by the researchers, 7) External Review which is the availability of the methodology used to conduct external review of the guideline and supporting evidence, and 8) Updating procedure, which is the procedure by which the guideline can be updated to incorporate new and emerging evidence and recommendations. Domain 3 ‘Rigor of Development’ scored 1.04%.

The fourth domain entitled ‘Clarity of Presentation’ is evaluated by 3 items including 1) Specific and Unambiguous Recommendations which clearly describes caveats and appropriate use cases are of the recommendations, based upon evidence, 2) Management Options which incorporates all options for clinical management within the guideline, and 3) Identifiable Key Recommendations which ensures key recommendations are presented in a way in which they are easily identifiable. Domain 4 ‘Clarity of Presentation’ scored 65.28%.

The fifth domain, entitled ‘Applicability’ is evaluated by 4 items including 1) Facilitators and Barriers to Application, which covers the issues with applying the guideline, 2) Implementation Advice/Tools which are incorporated within the guideline to aid implementation, 3) Resource Implications including cost, time, and materials required for implementation, and 4) Monitoring/Audit Criteria for evaluation of the success and consistency of application of the guideline. Domain 5 ‘Applicability’ was scored 0%.

The sixth and final domain, entitled ‘Editorial Independence’ is evaluated with 2 items entitled 1) Funding Body, concerning the sponsorship of the guideline’s development, and 2) Competing Interests which explicitly states the conflicting interests of the guidelines’ writers, financial or otherwise. Domain 6 ‘Editorial Independence’ also received a score of 0%.

All quality scores for the six appraised domains were low except for Domain 4: Clarity of Presentation (65.28%). A final scale rating overall guideline quality yielded a low score of 25%. Overall, three reviewers of four recommended the guideline for use if extensive modifications were made. In addition, the guideline received an overall low guideline quality rating of 25%.

Discussion

It is important to state how the development of COVID-19 clinical practice guidelines were likely developed within a very short timeframe while healthcare systems worked to manage care during an unprecedented crisis. With this in mind, appraisers suggest the lack of published supporting evidence and lack of explicit language describing a method for continual use as large contributors to poor appraisal scores. The low scores observed in Domains 1, 2, and 3 were attributed to a lack of available published content to support evidence-based development,

general ambiguity regarding guideline scope of use, and no mention of stakeholder involvement with development and implementation.

In developing future practice guidelines that will uphold the delivery of safe surgical and anesthesia care all reviewers deemed it is essential for guidelines to include source materials. Comments for these domains include: “No explanation of purpose was stated”. “The target audience is not clearly identified”, and “[There is an] unknown external review.” Additionally, guidelines intended to influence patient care outcomes should include explicit evidence and language stating the desired outcomes to provide greater transparency for clinician use.

Domain 4 encompassing the clarity of presentation was favorably scored by the reviewers. The guideline has an easy-to-read table format with clear and concise decision making guidelines, similar to an algorithm, however there can be ambiguity related to patient classification as ‘symptomatic’ or otherwise. Domains 5 and 6 lacked published supporting materials such as evidenced based literature, sourced data, financial implications, and peer review. When evaluated using the AGREE II format and domain examination, there was ambiguity regarding the intended future applicability and editorial independence of the guideline. Further additions of supporting evidence would ensure the SSCAC guidelines contribute to positive change in patient care. This appraisal serves as an opportunity to recommend change to existing clinical practice guidelines such as the SSCAC.

Limitations

Initially the project appraisal team for this project sought to collect data on the health outcomes of patients based on SSCAC provided by Corewell Health East (Appendix F, G). In embarking on this, it was recognized that data collection would not be feasible in part due to the ambiguity that challenged the research team in identifying appropriate data points with which to

collect data. The undefined development and implementation of the SSCAC paired with lack of an established time frame for data collection became fraught with additional variables. For example: COVID-19 vaccination status, COVID-19 variants, and selection of a suitable specific surgical patient population.

This guideline was created in response to inquiries from physicians and anesthesiologists after several articles were published providing recommendations pertaining to surgical scheduling and COVID-19. We understand the SSCAC was developed in an emergency situation to mitigate risk to patients and staff and was developed with an abundance of safety in mind. The reviewers also recognize that this guideline was developed in a short time frame under emergency conditions and thus it is understandable that it was labeled as 'considerations' rather than a formal guideline. Nevertheless, the 'considerations' were applied in such a way that they held the utilization of a guideline and were treated as such for over two years by the hospital system.

Conclusion

The low scores obtained from this quality improvement initiative highlight the importance of valid and transparent guidelines in the healthcare setting. Healthcare during the COVID-19 pandemic placed a spotlight on a weakness in the healthcare systems preparedness and ability to produce valid guidelines for streamlined care and importantly, patient safety.

Although the COVID-19 pandemic has been largely removed from influence within the hospital systems and the world is returning to normal, lessons from this guideline development and examination must be learned. If guidelines are to be developed for emergency implementation in the future, at the very least they should include availability of the evidence which they are based upon. They should be developed in a transparent manner in conjunction

with multiple specialties and current supporting evidence and avenues for improvement. Clinical practice guidelines must always be evidence based, and be thoroughly formulated with collaboration between multiple specialties. The low scores yielded by this appraisal highlight the complex work needed to produce valid guidelines which are needed to provide safe, competent, and up to date patient care.

By utilizing evidence based evaluation of the SSCAC with the AGREE II instrument, many lessons have been garnered regarding future establishments of surgical guidelines ;how future guideline development should occur using evidence based modalities, and how data collection regarding patient outcomes can be strengthened through the crucial process of guideline development at its start. The authors aim that through appraisal of SSCAC, recommendations for revision of the guideline will be rendered.

Given the evidence related to the long-term sequelae of COVID-19 infection, more specific research over the next few years will be necessary in continuation of establishing practice guidelines for surgical scheduling that allow safe administration of an anesthetic and recovery from surgery for patients infected with COVID-19.

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Appendix A: CHE-WBUH Surgical Scheduling Considerations after Covid 19

SURGICAL SCHEDULING CONSIDERATIONS AFTER COVID-19

SEVERITY OF ILLNESS DEFINITIONS		
1) MILD TO MODERATE • No Viral Pneumonia • 02 Sat. >94%	**2) SEVERE OR CRITICAL** • Pneumonia • Hypoxemic Failure • Septic Shock	**3) IMMUNOCOMPROMISED** • Special Consideration • Asymptomatic & Symptomatic Inclusion

A. *INFECTIVITY*: *GENERAL CDC RECOMMENDATIONS FOR DISCONTINUING ISOLATION AND OTHER TRANSMISSION RELATED PRECAUTIONS BASED ON SYMTPTOMS OF ALL SEVERITY OF ILLNESSES:*

1. At least 10 days have passed since symptoms first appeared
2. At least 24 hrs. have passed since last fever without fever-reducing meds
3. Symptoms (e.g. cough, SOB) have improved

SCENARIO	COVID-19 TESTING	SYMPTOMS	IMMUNOCOMPROMISED	D/C PRECAUTIONS
1	+	Asymptomatic	No	10 Days elapsed since 1st viral test
2	+	Mild to Moderate	No	General CDC Recommendation
3	+	Severe or Critical Illness ***OR***	Yes	General CDC Recommendation
4	Not Tested	Based on Symptoms		Based on Symptoms

*******10-20 Days Post + COVID-19, Consult with Infection Control Department******

B. *CONSIDERATIONS FOR POST COVID-19 TIMING OF SUGERY TO MINIMIZE RISK OF POST OPERATIVE COMPLICATION*

SCENARIO	WAIT TIME	SYMPTOMS
1	**4 Weeks**	Asymptomatic Pt. or Recovery from Mild, Non-Resp. Symptoms
2	**6 Weeks**	Symptomatic (e.g. cough, dyspnea) Who **Did Not** Require Hospitalization
3	**8 Weeks**	Symptomatic Pt. Who is Diabetic, Immunocompromised or Hospitalized and other co-morbidities
4	**12 Weeks**	Required Intensive Care or Progressive Care Admission or prolonged (>48hrs ??) High Flow Oxygen therapy

C. *VACCINATION CONSIDERATIONS FOR TIMING OF ELECTIVE SURGERY FROM DATE OF COVID-19 DIAGNOSIS*

1. Continue Pre-Op COVID Testing Even if Patient Has Been Vaccinated
2. If Possible, Avoid Surgery Between 1st and 2nd Vaccine Doses
3. To Ensure Full Immunity Consider Surgery 7-10 Days after 2nd dose.
4. If Patient is Experiencing Vaccine Related Adverse Effects, Cancel Surgery and Wait At Least 24-48 hrs. Before Re-Scheduling.

Appendix B: AGREE II Guidelines & AGREE II Instrument

Appendix to: Brouwers MC, Kho ME, Browman GP, et al.; the AGREE Next Steps Consortium.
AGREE II: Advancing guideline development, reporting and evaluation in health care. *CMAJ* 2010. DOI:10.1503/cmaj.090449. Copyright © 2009 The AGREE Research Trust

APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II

AGREE II

INSTRUMENT

The AGREE Next Steps Consortium

May 2009

SUGGESTED CITATION:
[PENDING]

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CIHR IRSC

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TABLE OF CONTENTS

I. INTRODUCTION

I. OVERVIEW

i) Purpose of the AGREE II Instrument

Clinical practice guidelines ('guidelines') are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances (1). In addition, guidelines can play an important role in health policy formation (2,3) and have evolved to cover topics across the health care continuum (e.g., health promotion, screening, diagnosis).

The potential benefits of guidelines are only as good as the quality of the guidelines themselves. Appropriate methodologies and rigorous strategies in the guideline development process are important for the successful implementation of the resulting recommendations (4-6). The quality of guidelines can be extremely variable and some often fall short of basic standards (7-9).

The *Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument* (10) was developed to address the issue of variability in guideline quality. To that end, the AGREE instrument is a tool that assesses the methodological rigour and transparency in which a guideline is developed. The original AGREE instrument has been refined, which has resulted in the new AGREE II and includes a new User's Manual (11).

The purpose of the AGREE II, is to provide a framework to:

1. assess the quality of guidelines;
2. provide a methodological strategy for the development of guidelines; and
3. inform what information and how information ought to be reported in guidelines.

The AGREE II replaces the original instrument as the preferred tool and can be used as part of an overall quality mandate aimed to improve health care.

ii) History of the AGREE Project

The original AGREE Instrument was published in 2003 by a group of international guideline developers and researchers, the AGREE Collaboration (10). The objective of the Collaboration was to develop a tool to assess the quality of guidelines. The AGREE Collaboration defined quality of guidelines *as the confidence that the potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice* (10). The assessment includes judgments about the methods used for developing the guidelines, the components of the final recommendations, and the factors that are linked to their uptake. The result of the Collaboration's effort was the original AGREE Instrument, a 23-item tool comprising 6 quality domains. The AGREE Instrument has been translated into many languages, has been cited in well over 100 publications, and is endorsed by several health care organizations. More details about the original instrument and related publications are available on the Web site of the AGREE Research Trust (http://www.agreetrust.org/), the official body managing the interests of the AGREE Instrument.

As with any new assessment tool, it was recognized that ongoing development was required to strengthen the measurement properties of the instrument and to ensure its usability and feasibility among intended users. This led several members of the original team to form the AGREE Next Steps Consortium (Consortium). The objectives of the Consortium were to further improve the measurement properties of the instrument, including its reliability and validity; to refine the instrument's items to better meet the needs of the intended users; and to improve the supporting documentation (i.e., original training manual and user's guide) to facilitate the ability of users to implement the instrument with confidence.

The result of these efforts is the AGREE II, which is comprised of the new User's Manual and 23 item tool organized into the same six domains, described here. The User's Manual is a significant modification of the original training manual and user's guide and provides explicit information for each of the 23 items. Table 1 compares the items of the original AGREE to the items in the AGREE II.

Table 1. Comparison of original AGREE and AGREE II items.

Original AGREE Item	AGREE II Item
Domain 1. Scope and Purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	No change
2. The clinical question(s) covered by the guideline is (are) specifically described.	The health question(s) covered by the guideline is (are) specifically described.
3. The patients to whom the guideline is meant to apply are specifically described.	The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
Domain 2. Stakeholder Involvement	
4. The guideline development group includes individuals from all the relevant professional groups.	No change
5. The patients' views and preferences have been sought.	The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.	No change
7. The guideline has been piloted among end users.	Delete item. Incorporated into user guide description of item 19.
Domain 3. Rigour of Development	
8. Systematic methods were used to search for evidence.	No change in item. Renumber to 7.
9. The criteria for selecting the evidence are clearly described.	No change in item. Renumber to 8.
	NEW Item 9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.	No change
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	No change
Original AGREE Item	**AGREE II Item**
12. There is an explicit link between the recommendations and the supporting evidence.	No change
13. The guideline has been externally reviewed by experts prior to its publication.	No change
14. A procedure for updating the guideline is provided.	No change
Domain 4. Clarity of Presentation	
15. The recommendations are specific and unambiguous.	No change
16. The different options for management of the condition are clearly presented.	The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.	No change
Domain 5. Applicability	
18. The guideline is supported with tools for application.	The guideline provides advice and/or tools on how the recommendations can be put into practice. AND Change in domain (from Clarity of Presentation) AND renumber to 19
19. The potential organizational barriers in applying the recommendations have been discussed.	The guideline describes facilitators and barriers to its application. AND change in order – renumber to 18
20. The potential cost implications of applying the recommendations have been considered.	The potential resource implications of applying the recommendations have been considered.
21. The guideline presents key review criteria for monitoring and/ or audit purposes.	The guideline presents monitoring and/ or auditing criteria.
Domain 6. Editorial Independence	
22. The guideline is editorially independent from the funding body.	The views of the funding body have not influenced the content of the guideline.
23. Conflicts of interest of guideline development members have been recorded.	Competing interests of guideline development group members have been recorded and addressed.

i) Which guidelines can be appraised with the AGREE II?

As with the original instrument, AGREE II is designed to assess guidelines developed by local, regional, national or international groups or affiliated governmental organizations. These include original versions of and updates of existing guidelines.

The AGREE II is generic and can be applied to guidelines in any disease area targeting any step in the health care continuum, including those for health promotion, public health, screening, diagnosis, treatment or interventions. It is suitable for guidelines presented in paper or electronic format. At this stage, the AGREE II has not been designed to assess the quality of guidance documents that address health care organizational issues. Its role in the assessment of health technology assessments has not yet been formally evaluated.

ii) Who can use the AGREE II?

The AGREE II is intended to be used by the following stakeholder groups:

- by **health care providers** who wish to undertake their own assessment of a guideline before adopting its recommendations into their practice;
- by **guideline developers** to follow a structured and rigorous development methodology, to conduct an internal assessment to ensure that their guidelines are sound, or to evaluate guidelines from other groups for potential adaptation to their own context;
- by **policy makers** to help them decide which guidelines could be recommended for use in practice or to inform policy decisions; and
- by **educators** to help enhance critical appraisal skills amongst health professionals and to teach core competencies in guideline development and reporting.

The AGREE Research Trust (ART) is an independent body established in 2004 at the conclusion of the activities of the original AGREE Collaboration. ART endorses the AGREE II and manages the interests of the AGREE enterprise, supports a research agenda regarding its development, and serves as the holder of its copyright.

The AGREE Research Trust web site http://www.agreetrust.org provides:

- free downloadable copies of AGREE II
- links to the AGREE II on-line training tool
- reference lists citing AGREE II and the original AGREE Instrument
- free downloadable copies of the original AGREE Instrument
- information about AGREE projects, the AGREE Next Steps Consortium and the original AGREE Collaboration

ii) How to cite the AGREE II

AGREE Next Steps Consortium (2009). *The AGREE II Instrument* [Electronic version]. Retrieved <Month, Day, Year>, from http://www.agreetrust.org .

iii) AGREE II On-Line Training Tool

For access to the AGREE II On-Line Training Tool, please visit http://www.agreetrust.org .

iv) References related to the AGREE II

AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Parallel publications in progress*

v) Primary reference related to the original AGREE Instrument

AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. *Qual Saf Health Care*. 2003 Feb;12(1):18-23.

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AGREE II:

USER'S MANUAL

II. USER'S MANUAL: INSTRUCTIONS FOR USING THE AGREE II

This User's Manual has been designed specifically to guide appraisers in the use of the instrument. We suggest reading the following instructions before using the instrument.

i) Accompanying Guideline Documents

Before applying the AGREE II, users should first carefully read the guideline document in full. In addition to the guideline document, users should attempt to identify all information about the guideline development process prior to the appraisal. This information may be contained in the same document as the guideline recommendations or it may be summarized in a separate technical report, methodological manual or guideline developer policy statement. These supporting documents may be published or may be available publicly on web sites. While it is the responsibility of the guideline authors to advise readers on the existence and location of relevant additional technical and supporting documents, every effort should be made by the AGREE II users to locate and include them as part of the materials appropriate for assessment.

ii) Number of Appraisers

We recommend that each guideline is assessed by at least 2 appraisers and preferably 4 as this will increase the reliability of the assessment. Reliability tests of the instrument are on-going.

The AGREE II consists of 23 key items organized within 6 domains followed by 2 global rating items ("Overall Assessment"). Each domain captures a unique dimension of guideline quality.

Domain 1. Scope and Purpose is concerned with the overall aim of the guideline, the specific health questions, and the target population (items 1-3).

Domain 2. Stakeholder Involvement focuses on the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users (items 4-6).

Domain 3. Rigour of Development relates to the process used to gather and synthesize the evidence, the methods to formulate the recommendations, and to update them (items 7-14).

Domain 4. Clarity of Presentation deals with the language, structure, and format of the guideline (items 15-17).

Domain 5. Applicability pertains to the likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline (items 18-21).

Domain 6. Editorial Independence is concerned with the formulation of recommendations not being unduly biased with competing interests (items 22-23).

Overall assessment includes the rating of the overall quality of the guideline and whether the guideline would be recommended for use in practice.

Each of the AGREE II items and the two global rating items are rated on a 7-point scale (1–strongly disagree to 7–strongly agree). The User's Manual provides guidance on how to rate each item using the rating scale and also includes 3 additional sections to further facilitate the user's assessment. The sections include User's Manual Description, Where to Look, and How to Rate.

i) Rating Scale

All AGREE II items are rated on the following 7-point scale:

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Score of 1 (*Strongly Disagree*). A score of 1 should be given when there is no information that is relevant to the AGREE II item or if the concept is very poorly reported.

Score of 7 (*Strongly Agree*). A score of 7 should be given if the quality of reporting is exceptional and where the full criteria and considerations articulated in the User's Manual have been met.

Scores between 2 and 6. A score between 2 and 6 is assigned when the reporting of the AGREE II item does not meet the full criteria or considerations. A score is assigned depending on the completeness and quality of reporting. Scores increase as more criteria are met and considerations addressed. The "How to Rate" section for each item includes details about assessment criteria and considerations specific to the item.

ii) User's Manual Description

This section defines the concept underlying the item in broad terms and provides examples.

iii) Where to Look

This section directs the appraiser to where the information in the guideline can usually be found. Included in this section are common terms used to label guideline sections or chapters. *These are suggestions only*. It is the responsibility of the appraiser to review the entire guideline and accompanying material(s) to ensure a fair evaluation.

iv) How to Rate

This section includes details about assessment criteria and considerations specific to each item.

- The *criteria* identify explicit elements that reflect the operational definition of the item. The more criteria that are met, the higher the score the guideline should receive on that item.
- The *considerations* are aimed to help inform the assessment. As in any evaluation, judgments by the appraisers are required. The more the considerations have been taken into account in the guideline, the higher the score the guideline should receive on that item.

It is important to note that guideline ratings require a level of judgment. The criteria and considerations are there to guide, not to replace, these judgments. Thus, none of the AGREE II items provide explicit expectations for each of the 7 points on the scale.

v) Other Considerations when Applying the AGREE II

On occasion, some AGREE II items may not be applicable to the particular guideline under review. For example, guidelines narrow in scope may not provide the full range of options for the management of the condition (see item 16). AGREE II does not include a "*Not Applicable*" response item in its scale. There are different strategies to manage this situation including having appraisers skip that item in the assessment process or rating the item as 1 (absence of information) and providing context about the score. *Regardless of strategy chosen, decisions should be made in advance, described in an explicit manner, and if items are skipped, appropriate modifications to calculating the domain scores should be implemented. As a principle, excluding items in the appraisal process is discouraged.*

A quality score is calculated for each of the six AGREE II domains. The six domain scores are independent and should not be aggregated into a single quality score.

i) Calculating Domain Scores

Domain scores are calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain.

Example:

If 4 appraisers give the following scores for Domain 1 (Scope & Purpose):

	Item 1	Item 2	Item 3	**Total**
Appraiser 1	5	6	6	**17**
Appraiser 2	6	6	7	**19**
Appraiser 3	2	4	3	**9**
Appraiser 4	3	3	2	**8**
Total	**16**	**19**	**18**	**53**

Maximum possible score = 7 (strongly agree) x 3 (items) x 4 (appraisers) = 84
Minimum possible score = 1 (strongly disagree) x 3 (items) x 4 (appraisers) = 12

The scaled domain score will be:

$$\frac{\text{Obtained score} - \text{Minimum possible score}}{\text{Maximum possible score} - \text{Minimum possible score}}$$

$$\frac{53 - 12}{84 - 12} \times 100 = \frac{41}{72} \times 100 = 0.5694 \times 100 = 57\ \%$$

If items are not included, appropriate modifications to the calculations of maximum and minimum possible scores are required.

ii) Interpreting Domain Scores

Although the domain scores are useful for comparing guidelines and will inform whether a guideline should be recommended for use, the Consortium has not set minimum domain scores or patterns of scores across domains to differentiate between high quality and poor quality guidelines. These decisions should be made by the user and guided by the context in which AGREE II is being used.

V. Overall Assessment

Upon completing the 23 items, AGREE II users will provide 2 overall assessments of the guideline. The overall assessment requires the user to make a judgment as to the quality of the guideline, taking into account the criteria considered in the assessment process. The user is also asked whether he/she would recommend use of the guideline.

The next pages include, by domain, guidance for rating each of the 23 items of the AGREE II when appraising a guideline. Each item includes a description, suggestions for where to find the item information, and guidance for how to rate.

DOMAIN 1. SCOPE AND PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

SCOPE AND PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

This deals with the potential health impact of a guideline on society and populations of patients or individuals. The overall objective(s) of the guideline should be described in detail and the expected health benefits from the guideline should be specific to the clinical problem or health topic. For example, specific statements would be:

- Preventing (long term) complications of patients with diabetes mellitus
- Lowering the risk of subsequent vascular events in patients with previous myocardial infarction
- Most effective population-based colorectal screening strategies
- Providing guidance on the most effective therapeutic treatment and management of patients with diabetes mellitus.

Where to Look:

Examine the opening paragraphs/chapters for a description of the scope and purpose of the guideline. In some cases, the rationale or need for the guideline is described in a document separate from the guideline, for instance, in the guideline proposal. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: introduction, scope, purpose, rationale, background, and objectives.

How to Rate:

Item content includes the following *CRITERIA:*

- health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.)
- expected benefit or outcome
- target(s) (e.g., patient population, society)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?

SCOPE AND PURPOSE

2. The health question(s) covered by the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A detailed description of the health questions covered by the guideline should be provided, particularly for the key recommendations (see Item 17), although they need not be phrased as questions. Following the examples provided in question 1:

- How many times a year should the HbA1c be measured in patients with diabetes mellitus?
- What should the daily aspirin dosage for patients with proven acute myocardial infarction be?
- Does population-based colorectal screening using the fecal occult blood test reduce mortality of colorectal cancer?
- Is self-monitoring effective for blood glucose control in patients with Type 2 diabetes?

Where to Look:

Examine the opening paragraphs/chapters for a description of the scope and purpose of the guideline. In some cases, the questions are described in a document separate from the guideline, for instance in a search specification. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: questions, scope, purpose, rationale, and background.

How to Rate:

Item content includes the following *CRITERIA:*

- target population
- intervention(s) or exposure(s)
- comparisons (if appropriate)
- outcome(s)
- health care setting or context

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is there enough information provided in the question(s) for anyone to initiate the development of a guideline on this topic or to understand the patients/populations and contexts profiled in the guideline?

SCOPE AND PURPOSE

3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A clear description of the population (i.e., patients, public, etc.) covered by a guideline should be provided. The age range, sex, clinical description, and comorbidity may be provided. For example:

- A guideline on the management of diabetes mellitus only includes patients with non-insulin dependent diabetes mellitus and excludes patients with cardiovascular comorbidity.
- A guideline on the management of depression only includes patients with major depression according to the DSM-IV criteria, and excludes patients with psychotic symptoms and children.
- A guideline on screening of breast cancer only includes women, aged between 50 and 70 years, with no history of cancer and with no family history of breast cancer.

Where to Look:

Examine the opening paragraphs/chapters for a description of the target population of the guideline. The explicit exclusion of some populations (for instance children) is also covered by this item. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: patient population, target population, relevant patients, scope, and purpose.

How to Rate: Item content includes the following *CRITERIA:*

- target population, gender and age
- clinical condition (if relevant)
- severity/stage of disease (if relevant)
- comorbidities (if relevant)
- excluded populations (if relevant)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is the population information specific enough so that the correct and eligible individuals would receive the action recommended in the guideline?

DOMAIN 2. STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.

STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

This item refers to the professionals who were involved at some stage of the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations. *This item excludes individuals who have externally reviewed the guideline (see Item 13). This item excludes target population representation (see Item 5).* Information about the composition, discipline, and relevant expertise of the guideline development group should be provided.

Where to Look:

Examine the opening paragraphs/chapters, acknowledgement section or appendices for the composition of the guideline development group. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, guideline panel member list, acknowledgements, and appendices.

How to Rate:

Item content includes the following *CRITERIA:*

- For each member of the guideline development group, the following information is included:
  - name
  - discipline/content expertise (e.g., neurosurgeon, methodologist)
  - institution (e.g., St. Peter's hospital)
  - geographical location (e.g., Seattle, WA)
  - a description of the member's role in the guideline development group

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Are the members an appropriate match for the topic and scope? Potential candidates include relevant clinicians, content experts, researchers, policy makers, clinical administrators, and funders.
- Is there at least one methodology expert included in the development group (e.g., systematic review expert, epidemiologist, statistician, library scientist, etc.)?

STAKEHOLDER INVOLVEMENT

5. The views and preferences of the target population (patients, public, etc.) have been sought. v and preferences have been sought.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Information about target population experiences and expectations of health care should inform the development of guidelines. There are various methods for ensuring that these perspectives inform the different stages of guideline development by stakeholders. For example, formal consultations with patients/public to determine priority topics, participation of these stakeholders on the guideline development group, or external review by these stakeholders on draft documents. Alternatively, information could be obtained from interviews of these stakeholders or from literature reviews of patient/public values, preferences or experiences. There should be evidence that some process has taken place and that stakeholders' views have been considered.

Where to Look:

Examine the paragraphs on the guideline development process. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: scope, methods, guideline panel member list, external review, and target population perspectives.

How to Rate: **Item content includes the**

following *CRITERIA:*

- statement of type of strategy used to capture patients'/public's' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences)
- methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups)
- outcomes/information gathered on patient/public information
- description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?

6. The target users of the guideline are clearly defined.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

The target users should be clearly defined in the guideline, so the reader can immediately determine if the guideline is relevant to them. For example, the target users for a guideline on low back pain may include general practitioners, neurologists, orthopaedic surgeons, rheumatologists, and physiotherapists.

Where to Look:

Examine the opening paragraphs/chapters for a description of the target users of the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: target user and intended user.

How to Rate: **Item content includes the**

following *CRITERIA:*

- clear description of intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators)
- description of how the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Are the target users appropriate for the scope of the guideline?

DOMAIN 3. RIGOUR OF DEVELOPMENT

7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.

7. Systematic methods were used to search for evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Details of the strategy used to search for evidence should be provided including search terms used, sources consulted, and dates of the literature covered. Sources may include electronic databases (e.g. MEDLINE, EMBASE, CINAHL), databases of systematic reviews (e.g. the Cochrane Library, DARE), handsearching journals, reviewing conference proceedings, and other guidelines (e.g. the US National Guideline Clearinghouse, the German Guidelines Clearinghouse). The search strategy should be as comprehensive as possible and executed in a manner free from potential biases and sufficiently detailed to be replicated.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process. In some cases the search strategies are described in separate documents or in an appendix to the guideline. Examples of commonly labelled sections or chapters in a guideline where this information can be found include: methods, literature search strategy, and appendices.

How to Rate:

Item content includes the following *CRITERIA:*

- named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL)
- time periods searched (e.g., January 1, 2004 to March 31, 2008)
- search terms used (e.g., text words, indexing terms, subheadings)
- full search strategy included (e.g., possibly located in appendix)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is the search relevant and appropriate to answer the health question? (e.g., all relevant databases and, appropriate search terms used)
- Is there enough information provided for anyone to replicate the search?

8. The criteria for selecting the evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Criteria for including/excluding evidence identified by the search should be provided. These criteria should be explicitly described and reasons for including and excluding evidence should be clearly stated. For example, guideline authors may decide to only include evidence from randomized clinical trials and to exclude articles not written in English.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process. In some cases, the inclusion or exclusion criteria for selecting the evidence are described in separate documents or in an Appendix to the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, literature search, inclusion/exclusion criteria, and appendices.

How to Rate:

Item content includes the following *CRITERIA:*

- description of the inclusion criteria, including
  - target population (patient, public, etc.) characteristics
  - study design
  - comparisons (if relevant)
  - outcomes
  - language (if relevant) ➢ context (if relevant)
- description of the exclusion criteria (if relevant; e.g., *French only* listed in the inclusion criteria statement could logically preclude *non-French* listed in the exclusion criteria statement)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is there a rationale given for the chosen inclusion/exclusion criteria?
  - Do inclusion/exclusion criteria align with the health question(s)?
- Are there reasons to believe that relevant literature may not have been considered?

9. The strengths and limitations of the body of evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Statements highlighting the strengths and limitations of the evidence should be provided. This ought to include explicit descriptions - using informal or formal tools/methods - to assess and describe the risk of bias for individual studies and/or for specific outcomes and/or explicit commentary of the body of evidence aggregated across all studies. This may be presented in different ways, for example: using tables commenting on different quality domains; the application of a formal instrument or strategy (e.g., Jadad scale, GRADE method); or descriptions in the text.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process for information on how the methodological quality of the studies (e.g., risk of bias) were described. Evidence tables are often used to summarize quality features. Some guidelines make a clear distinction between description and interpretation of evidence, for instance, in a results section and a discussion section, respectively.

How to Rate:

Item content includes the following *CRITERIA:*

- descriptions of how the body of evidence was evaluated for bias and how it was interpreted by members of the guideline development group

- aspects upon which to frame descriptions include:
  - study design(s) included in body of evidence
  - study methodology limitations (sampling, blinding, allocation concealment, analytical methods)
  - appropriateness/relevance of primary and secondary outcomes considered
  - consistency of results across studies
  - direction of results across studies
  - magnitude of benefit versus magnitude of harm
  - applicability to practice context

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Are the descriptions appropriate, neutral, and unbiased? Are the descriptions complete?

10. The methods for formulating the recommendations are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A description of the methods used to formulate the recommendations and how final decisions were arrived at should be provided. For example, methods may include a voting system, informal consensus, and formal consensus techniques (e.g., Delphi, Glaser techniques). Areas of disagreement and methods of resolving them should be specified.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process. In some cases, the methods used to formulate the recommendations are described in separate documents or in an appendix to the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include methods and guideline development process.

RIGOUR OF DEVELOPMENT

11. The health benefits, side effects, and risks have been considered in formulating the recommendations.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

The guideline should consider health benefits, side effects, and risks when formulating the recommendations. For example, a guideline on the management of breast cancer may include a discussion on the overall effects on various final outcomes. These may include: survival, quality of life, adverse effects, and symptom management or a discussion comparing one treatment option to another. There should be evidence that these issues have been addressed.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process for a description of the body of evidence, its interpretation, and the translation to practice recommendations. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, interpretation, discussion, and recommendations.

How to Rate:

Item content includes the following *CRITERIA:*

- supporting data and report of benefits
- supporting data and report of harms/side effects/risks
- reporting of the balance/trade-off between benefits and harms/side effects/risks
- recommendations reflect considerations of both benefits and harms/side effects/risks

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is the discussion an integral part of the guideline development process? (i.e., taking place during recommendation formulation rather than post-formulation as an afterthought). - Has the guideline development group considered the benefits and harms equally?

25

27

How to Rate:

Item content includes the following *CRITERIA:*

- description of the recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered)
- outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures)
- description of how the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Was a formal process used to arrive at the recommendations?
- Were the methods appropriate?

24

How to Rate:

Item content includes the following *CRITERIA:*

- supporting data and report of benefits
- supporting data and report of harms/side effects/risks
- reporting of the balance/trade-off between benefits and harms/side effects/risks
- recommendations reflect considerations of both benefits and harms/side effects/risks

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is the discussion an integral part of the guideline development process? (i.e., taking place during recommendation formulation rather than post-formulation as an afterthought) - Has the guideline development group considered the benefits and harms equally?

RIGOUR OF DEVELOPMENT

12. There is an explicit link between the recommendations and the supporting evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

An explicit link between the recommendations and the evidence on which they are based should be included in the guideline. The guideline user should be able to identify the components of the body of evidence relevant to each recommendation.

Where to Look:

Define and examine the recommendations in the guideline and the text describing the body of evidence that underpins them. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations and key evidence.

How to Rate:

Item content includes the following *CRITERIA:*

- the guideline describes how the guideline development group linked and used the evidence to inform recommendations
- each recommendation is linked to a key evidence description/paragraph and/or reference list
- recommendations linked to evidence summaries, evidence tables in the results section of the guideline

Additional *CONSIDERATIONS*:

- Is there congruency between the evidence and recommendations?
- Is the link between the recommendations and supporting evidence easy to find in the guideline?
- When evidence is lacking or a recommendation is informed primarily by consensus of opinion by the guideline group, rather than the evidence, is this clearly stated and described?

RIGOUR OF DEVELOPMENT

13. The guideline has been externally reviewed by experts prior to its publication.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A guideline should be reviewed externally before it is published. Reviewers should not have been involved in the guideline development group. Reviewers should include experts in the clinical area as well as some methodological experts. Target population (patients, public) representatives may also be included. A description of the methodology used to conduct the external review should be presented, which may include a list of the reviewers and their affiliation.

Where to Look:

Examine the paragraphs/chapters describing the guideline development process and the acknowledgement section. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, results, interpretation, and acknowledgements.

How to Rate:

Item content includes the following *CRITERIA:*

- purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence)
- methods taken to undertake the external review (e.g., rating scale, open-ended questions)
- description of the external reviewers (e.g., number, type of reviewers, affiliations)
- outcomes/information gathered from the external review (e.g., summary of key findings)
- description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Are the external reviewers relevant and appropriate to the scope of the guideline? Was there a rationale given for choosing the included reviewers?
- How was information from the external review used by the guideline development group?

14. A ocedure for updating the guideline is provided.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Guidelines need to reflect current research. A clear statement about the procedure for updating the guideline should be provided. For example, a timescale has been given or a standing panel is established who receives regularly updated literature searches and makes changes as required.

Where to Look:

Examine the introduction paragraph, the paragraphs describing the guideline development process and the closing paragraphs. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, guideline update, and date of guideline.

How to Rate:

Item content includes the following *CRITERIA:*

- a statement that the guideline will be updated
- explicit time interval or explicit criteria to guide decisions about when an update will occur
- methodology for the updating procedure is reported

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is there enough information provided to know when an update will occur or what criteria would trigger an update?

DOMAIN 4. CLARITY OF PRESENTATION

15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.

15. The recommendations are specific and unambiguous.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A recommendation should provide a concrete and precise description of which option is appropriate in which situation and in what population group, as informed by the body of evidence.

- An example of a specific recommendation is: Antibiotics should be prescribed in children two years or older with a diagnosis of acute otitis media if the pain lasts longer than three days or if the pain increases after the consultation despite adequate treatment with painkillers; in these cases, amoxicillin should be given for 7 days (supplied with a dosage scheme).
- An example of a vague recommendation is: Antibiotics are indicated for cases with an abnormal or complicated course.

It is important to note that in some instances, evidence is not always clear cut and there may be uncertainty about the best care option(s). In this case, the uncertainty should be stated in the guideline.

Where to Look:

Define and examine the recommendations in the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations and executive summary.

How to Rate:

Item content includes the following *CRITERIA:*

- statement of the recommended action
- identification of the intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects)
- identification of the relevant population (e.g., patients, public)

- caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply)

Additional *CONSIDERATIONS*:

- In the event of multiple recommendations (e.g., management guidelines), is there clarity regarding to whom each recommendation applies?
- If there is uncertainty in the interpretation and discussion of the evidence, is the uncertainty reflected in the recommendations and explicitly stated?

CLARITY OF PRESENTATION

16. The different options for management of the condition or health issue are clearly presented.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

A guideline that targets the management of a disease should consider the different possible options for screening, prevention, diagnosis or treatment of the condition it covers. These possible options should be clearly presented in the guideline.
For example, a recommendation on the management of depression may contain the following treatment alternatives:
a. Treatment with TCA
b. Treatment with SSRI
c. Psychotherapy
d. Combination of pharmacological and psychological therapy

Where to Look:

Examine the recommendations and their supporting evidence. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: executive summary, recommendations, discussion, treatment options, and treatment alternatives.

How to Rate:

Item content includes the following *CRITERIA:*

- description of options
- description of population or clinical situation most appropriate to each option

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is this pertaining to a guideline broad or narrow in scope? This item may be more relevant to guidelines that are broad in scope (e.g., covering the management of a condition or issue rather than focusing on a particular set of interventions for a specific condition/issue).

17. Key recommendations are easily identifiable.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Users should be able to find the most relevant recommendations easily. These recommendations answer the main question(s) that have been covered by the guideline and can be identified in different ways. For example, they can be summarized in a box, typed in bold, underlined or presented as flow charts or algorithms.

Where to Look:

Examples of commonly labeled sections or chapters in a guideline where this information can be found include: executive summary, conclusions, and recommendations. Some guidelines provide separate summaries with key recommendations (e.g., quick reference guide).

How to Rate:

Item content includes the following *CRITERIA:*

- description of recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms
- specific recommendations are grouped together in one section

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?

- Are the key recommendations appropriately selected and do they reflect the key messages of the guideline?
- Are specific recommendations grouped in a section placed near the summary of the key evidence?

DOMAIN 5. APPLICABILITY

18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.

18. The guideline describes facilitators and barriers to its application.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

There may be existing facilitators and barriers that will impact the application of guideline recommendations. For example:

i. A guideline on stroke may recommend that care should be coordinated through stroke units and stroke services. There may be a special funding mechanism in the region to enable the formation of stroke units.

ii. A guideline on diabetes in primary care may require that patients are seen and followed up in diabetic clinics. There may be an insufficient number of clinicians available in a region to enable clinics to be established.

Where to Look:

Examine the paragraph/chapter on the dissemination/implementation of the guideline or, if available, additional documents with specific plans or strategies for implementation of the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: barriers, guideline utilization, and quality indicators.

How to Rate:

Item content includes the following *CRITERIA:*

- identification of the types of facilitators and barriers that were considered
- methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation)
- information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography)
- description of how the information influenced the guideline development process and/or formation of the recommendations

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Does the guideline suggest specific strategies to overcoming the barriers?

APPLICABILITY

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

For a guideline to be effective it needs to be disseminated and implemented with additional materials. For example, these may include: a summary document, a quick reference guide, educational tools, results from a pilot test, patient leaflets, or computer support. Any additional materials should be provided with the guideline.

Where to Look:

Examine the paragraph on the dissemination/implementation of the guideline and, if available, the specific accompanying materials that have been produced to support the dissemination and implementation of the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: tools, resources, implementation, and appendices.

How to Rate:

Item content includes the following *CRITERIA:*

- an implementation section in the guideline
- tools and resources to facilitate application:
  - guideline summary documents
  - links to check lists, algorithms
  - links to how-to manuals
  - solutions linked to barrier analysis (see Item 18)
  - tools to capitalize on guideline facilitators (see Item 18)
  - outcome of pilot test and lessons learned
- directions on how users can access tools and resources

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- Is there information about the development of the implementation tools and validation procedures?

APPLICABILITY

20. The potential resource implications of applying the recommendations have been considered.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

The recommendations may require additional resources in order to be applied. For example, there may be a need for more specialized staff, new equipment, and expensive drug treatment. These may have cost implications for health care budgets. There should be a discussion in the guideline of the potential impact of the recommendations on resources.

Where to Look:

Examine the paragraph(s) on the dissemination/implementation of the guideline or, if available, additional documents with specific plans or strategies for implementation of the guideline. Some guidelines present cost implications in the paragraphs that discuss the evidence or decisions behind the recommendations. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, cost utility, cost effectiveness, acquisition costs, and implications for budgets.

How to Rate:

Item content includes the following *CRITERIA:*

- identification of the types of cost information that were considered (e.g., economic evaluations, drug acquisition costs)
- methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.)
- information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course)
- description of how the information gathered was used to inform the guideline development process and/or formation of the recommendations

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?

- Were appropriate experts involved in finding and analyzing the cost information?

APPLICABILITY

21. The guideline presents monitoring and/or auditing criteria.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Measuring the application of guideline recommendations can facilitate their ongoing use. This requires clearly defined criteria that are derived from the key recommendations in the guideline. The criteria may include process measures, behavioral measures, clinical or health outcome measures. Examples of monitoring and audit criteria are:

- The HbA1c should be < 8.0%.
- The level of diastolic blood pressure should be < 95 mmHg.
- 80% of the population aged 50 years should receive colorectal cancer screening rates using fecal occult blood tests.
- If complaints of acute otitis media last longer than three days, amoxicillin should be prescribed.

Where to Look:

Examine the paragraph/chapter on auditing or monitoring the use of the guideline or, if available, additional documents with specific plans or strategies for evaluation of the guideline. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: recommendations, quality indicators, and audit criteria.

How to Rate:

Item content includes the following *CRITERIA:*

- identification of criteria to assess guideline implementation or adherence to recommendations
- criteria for assessing impact of implementing the recommendations
- advice on the frequency and interval of measurement
- descriptions or operational definitions of how the criteria should be measured

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?

- Are a range of criteria provided including process measures, behavioural measures, and clinical or health outcomes?

DOMAIN 6. EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.

EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

Many guidelines are developed with external funding (e.g., government, professional associations, charity organizations, pharmaceutical companies). Support may be in the form of financial contribution for the complete development, or for parts of it (e.g., printing of the guidelines). There should be an explicit statement that the views or interests of the funding body have not influenced the final recommendations.

Where to Look:

Examine the paragraphs/chapters on the guideline development process or acknowledgements section. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: disclaimer and funding source.

How to Rate:

Item content includes the following *CRITERIA*:

- the name of the funding body or source of funding (or explicit statement of no funding)
- a statement that the funding body did not influence the content of the guideline

Additional *CONSIDERATIONS*:

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- How did the guideline development group address potential influence from the funding body?

EDITORIAL INDEPENDENCE

23. Competing interests of guideline development group members have been recorded and addressed.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

User's Manual Description:

There are circumstances when members of the development group may have competing interests. For example, this would apply to a member of the development group whose research on the topic covered by the guideline is also funded by a pharmaceutical company. There should be an explicit statement that all group members have declared whether they have any competing interests.

Where to Look:

Examine the paragraphs/chapters describing the guideline development group or acknowledgements section. Examples of commonly labeled sections or chapters in a guideline where this information can be found include: methods, conflicts of interest, guideline panel, and appendix.

How to Rate:

Item content includes the following *CRITERIA:*

- description of the types of competing interests considered
- methods by which potential competing interests were sought
- description of the competing interests
- description of how the competing interests influenced the guideline process and development of recommendations

Additional *CONSIDERATIONS:*

- Is the item well written? Are the descriptions clear and concise?
- Is the item content easy to find in the guideline?
- What measures were taken to minimize the influence of competing interests on guideline development or formulation of the recommendations?

OVERALL GUIDELINE ASSESSMENT

OVERALL GUIDELINE ASSESSMENT

For each question, please choose the response which best characterizes the guideline assessed:

1. Rate the overall quality of this guideline.						
1 Lowest possible quality	2	3	4	5	6	7 Highest possible quality

2. I would recommend this guideline for use.	
Yes	
Yes, with modifications	
No	

NOTES

User's Manual Description:

The overall assessment requires the AGREE II user to make a judgment as to the quality of the guideline, taking into account the appraisal items considered in the assessment process.

AGREE II INSTRUMENT

DOMAIN 1. SCOPE AND PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

2. The health question(s) covered by the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 2. STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

5. The views and preferences of the target population (patients, public, etc.) have been sought.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

6. The target users of the guideline are clearly defined.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 3. RIGOUR OF DEVELOPMENT

7. Systematic methods were used to search for evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

8. The criteria for selecting the evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

9. The strengths and limitations of the body of evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 3. RIGOUR OF DEVELOPMENT continued

10. The methods for formulating the recommendations are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

11. The health benefits, side effects, and risks have been considered in formulating the recommendations.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

12. There is an explicit link between the recommendations and the supporting evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 3. RIGOUR OF DEVELOPMENT continued

13. The guideline has been externally reviewed by experts prior to its publication.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

14. A procedure for updating the guideline is provided.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

8

15. T recommendations are specific and unambiguous.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

16. The different option for management of the issue condition or health are clearly presented.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 5. APPLICABILITY

17. Key recommendations are easily identifiable.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

9

Comments

18. The guideline describes facilitators and barriers to its application.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

20. The potential resource implications of applying the recommendations have been considered.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

21. The guideline presents monitoring and/or auditing criteria.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 6. EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

12

Comments

23. Competing interests of guideline development group members have been recorded and addressed.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

13

OVERALL GUIDELINE ASSESSMENT

For each question, please choose the response which best characterizes the guideline assessed:

1. Rate the overall quality of this guideline.

1 Lowest possible quality	2	3	4	5	6	7 Highest possible quality

2. I would recommend this guideline for use.

Yes	
Yes, with modifications	
No	

NOTES

Appendix C: AGREE Reporting Checklist

AGREE Reporting Checklist
2016

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☐ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☐ Target(s) (e.g., patient population, society)	
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☐ Target population ☐ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☐ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	☐ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☐ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☐ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☐ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	

DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☐ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☐ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☐ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☐ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☐ Supporting data and report of benefits ☐ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/risks	
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	

13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☐ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☐ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☐ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☐ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the	

	population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☐ Additional materials to support the implementation of the guideline in practice. For example: ◻ Guideline summary documents ◻ Links to check lists, algorithms ◻ Links to how-to manuals ◻ Solutions linked to barrier analysis (see Item 18) ◻ Tools to capitalize on guideline facilitators (see Item 18) ◻ Outcome of pilot test and lessons learned	
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	

From:
Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at www.agreetrust.org.

Appendix D: Evaluation & Synthesis Table

Author (Year)	Conceptual Framework	Design/Method	Sample/Setting	Major Variables Studied	Measurement	Data Analysis	Findings	Appraisal: Worth to Practice
1. Cohen et al, (2020). Journal of clinical hypertension: 22(10)	None	**RCT** Purpose: Evaluate the effect of continuation vs. discontinuation of ACE or ARBS in COVID patients Hierarchical composite scoring of hospital related outcomes (time to death, duration of mv, duration of rrt, duration of vp, measures of multiorgan dysfunction.)	n= 136 → 152 needed Adult patients admitted with COVID-19	Time to all cause death, hospital length of stay, length of ICU stay, MV, hypotension requiring vasopressors, change in serum Cr, AKI, readmissions, major cardiac events.	Modified SOFA score, global rank score	Wilcoxon rank-sum test Linear regression analysis	Pending	**Weaknesses:** -Trial has not been completed yet due to further participants needed (15 still needed). **Strengths:** -Detailed planned statistical analysis - Logical design and organization of variables **Conclusion:**- The REPLACE COVID trial has a promising design, and the researchers hope its future results will provide vital information surrounding cardiac involvement in COVID patients.

2. Hirata, N. & Yamakage, M. (2021). Journal of Anesthesia, 35	None	**Expert Opinion** Purpose: Special article intended to highlight important perioperative cardiovascular considerations during the COVID-19 pandemic.	Expert opinion highlighting the epidemiology, prognosis, infectious mechanism, and guidelines for cardiac management of patients with a diagnosis of COVID-19.	Myocardial injury, case fatality rate, cardiomyopathy, cardiac troponin levels, BNP levels, + SARS CO-V present in human heart autopsy samples, septic myocardial dysfunction, hypercoagulation, ACE2 levels in blood	Article summarizes various case reports of COVID related cardiology studies.	Review article summarizes current findings but does not include primary research.	The number of surgical patients with COVID-19 will continue to increase. Little established evidence displaying the effects that anesthesia and surgery has on COVID, the anesthesiologist needs to recognize COVID related CV concerns	**Weaknesses:** -Not primary research, limited data or studies yet available/ **Strengths:** -Article supports the researcher's theory and research question directly. **Conclusion:** -Excellent article to include in this integrative review because although it does not provide primary data, article describes the exact concerns of the researchers hypothesis

3. Huang et al, (2020). Journal of the American College of Cardiology ,13(11)	None	**Retrospective Observational Study** Purpose: Evaluate cardiac involvement in patients recovered from COVID-19 Tongji Hospital, Tongji Medical College, Wuhan, China.	n= 26 who reported cardiac symptoms underwent CMR s/p COVID-19 infection	Edema ratio LGE Cardiac function Native T1/T2 ECV	SPSS Shapiro-Wilk test Median Interquartile Range Mean SD	T1, T2, and ECV were all found to be sig. elevated in patients with positive conventional CMR findings, compared with patients without positive findings and controls.	Cardiac involvement was found in a proportion of patients recovered from COVID-19 → n=15, 58%). Myocardial edema n=14 54% CMR manifestation included myocardial edema, fibrosis, and impaired right ventricle function.	**Weaknesses:** -Small study -Focus of symptomatic patients only (future surgical patients may not be symptomatic) **Strengths:** Outcome measures consistent and reliable Study Measures cardiac involvement in "recovered" patients, key for examining prolonged involvement of COVID-19 in cardiology. **Conclusion:** Article supports researcher's hypothesis directly, provides a strong foundation for research project.

4. Sivalogana et al, (2020). British journal of haematolo gy, 190(4)	None	**RCT** Purpose: Determine if antithrombotic therapy decreases mortality in COVID-19 patients, by counteracting the known coagulopathic effects of the SARS-COV-2 virus Performed at Brighton and Sussex University Hospital	<u>Antiplatelet Group</u> n= 29 62% (n=18) were on aspirin 28% (n=8) 45 on clopidogrel 10% (n=3) on both Matched to controls n=58 <u>Anticoagulant Group</u> n= 31 23% (n=7) were on warfarin, 39% (n=12) apixaban, 3% (n=1) dabigatran, 6% low molecular weight heparin (n=2), and 29% (n=9) rivaroxaban. Matched to controls (n=62).	COVID-19 mortality Thrombotic disorders	SD Log-Rank Test SPSS Kaplan-Meier Curves Wilcoxon rank sum tests	SD for antiplatelet: 80 (9.2) SD for Anticoagula nt: 79 (11.6) r	Patients on aspirin downtrended mortality, patients on warfarin uptrended mortality. Shows that patients taking antithrombotic therapy at the time of infection with COVID-19 do not have significantly different mortality risk to those patients not taking antithrombotic therapy.	**Weaknesses:** Small study, Limited sample size did not allow for statistical significance to be achieved. **Strengths:** Study shows no increase effect in mortality. Shows larger scale investigation still needed. **Conclusion:** Further research needed.

5. Mitrani, R. D. et al., (2020).	None	**Expert Opinion Purpose:** To establish methods and criteria for long term cardiac evaluation of patients who exhibited cardiac symptoms during a COVID-19 infection.	An estimated 20-30% of patients hospitalized with COVID-19 had evidence of myocardial involvement via elevated troponin levels. There are currently no long-term data on cardiovascular abnormalities or dysrhytmias presenting long term.	Multiple pathway to cardiac injury: MI, myocarditis, vasculitis, inflammation, thrombosis, stress.	Increases in myocardial disease sequelae and increased morbidity and mortality from cardiovascular complications in the future.	Similar mechanisms of injury seen during COVID would warrant future monitoring if not within the COVID-19 setting, future sequelae are not able to be predicted at this time, so future recurrence or morbidity is not predictable.	In patients recovered from myocardial injury such as MI or myocarditis, subclinical and overt cardiac abnormalities are expected in some patients. This is no different in COVID-19 which may present in patients with no other cardiac insult. Future monitoring and evaluation are required.	**Weaknesses:** Not experimental in design and no studies overtly done to examine long term effects of cardiac insult during COVID-19. **Strengths:** Exhaustively examines pathophysiology of cardiac insult in COVID-19 and relates to non-COVID-19 injury, citing follow up examination without COVID infection should be carried over at minimum to those patients with cardiac insult resulting from COVID-19. **Conclusion:** Further studies examining cardiac status of patients recovering from COVID-19 are necessary as a great risk presents to patients with unresolved cardiac function.

6. Sattar, Y. et al., (2020)**.**	None	**Background Information Purpose:** Establish a background for the pathophysiologies of various cardiac complications that have occurred due to COVID-19.	This article has collaborated many case reports, studies, and experimental examinations of the novel coronavirus into one format to discuss cardiac involvement in COVID-19 infection.	Cardiovascular cellular pathogenesis, i.e. electrical dysfunction and arrhythmias, mechanical dysfunction, vascular and valvular damage, and possible treatment.	Observational and dissertational in nature. Case and cohort studies data reporting.	Data collection from various case studies, integration with current knowledge and literature pertaining to cardiac disease.	The pathophysiology of COVID-19 induced cardiac complications varies very little from other etiologies and still poses similar risks to non-COVID-19 induced cardiac complications. Hypercoagulability of COVID patients poses them at a higher risk of thrombotic injury, the effects of which remain the same to other etiologies of thrombotic cardiac injury. Mast activation and ACE2 upregulation may lead to valvular and myocardial wall changes.	**Weaknesses:** Informational and collaborative in nature with no independent study or experiment. **Strengths:** Broad scope of myocardial injury pathophysiology, with current recommended treatments and effects. **Conclusion:** With the exception of ACE2 upregulation and COVID-19 affinity for the receptor, pathophysiology of cardiac insult during COVID-19 does not differ from other etiologies. Further research into randomized controlled data regarding cardiac injury, treatment, and post evaluation must be completed.

7. Khalid, Y. et al., (2020).	None	**Case Report Purpose:** A single case report of COVID-19 myocarditis presenting as Takotsubo cardiomyopathy (stress induced). Cardiac injury presented via direct injury from COVID-19	A single case examination with cardiac abnormalities attributed directly to COVID-19.	A complete laboratory panel, along with TEE and 2DECHO for LVEF status, IL2 and other biomarkers were measured. Medication treatment plan and level of care included.	Laboratory values tracked along with troponin give the ability to pinpoint when cardiac insult occurred. The presence of NSTEMI with QTc elongation, increased cardiac enzymes, right and left ventricular hypodamics and decreased LVEF.	The patient presented with signs and symptoms of Takotsubo myopathy with a concurrent viral infection	Recurrent TEE showed a reduced EF by 50% due to viral cardiomyopathy with right and septal wall hypodynamics, indicating a more inclusive pathology of viral cardiomyopathy in the setting of COVID-19 compounded by NSTEMI.	**Weaknesses:** A single case review may not be representative of an entire population. **Strengths:** Very detailed laboratory panel and procedural results with imaging included. Explanation of patient conditions, care and treatment plan. **Conclusion:** Given the detailed presentation, links between this case and other pathologies can be made to establish the presence and possibility of long term myocardial injury due to viral cardiomyopathy. Concurrence with other research is required.

8. Sala, S. et al., (2020)**.**	None	**Case Report Purpose:** A single case report of a COVID-19 myocarditis presenting as reverse tako-tsubo syndrome. Lymphocytic cardiomyopathy diagnosed vs. acute viral cardiomyopathy.	A single case examination with cardiac abnormalities attributed directly to COVID-19 in a presentation other than viral cardiomyopathy.	A complete laboratory panel, along with CXR, ECG, CTA, CMR, TEE, and 2DECHO for LVEF status, IL2 and other biomarkers were measured.	CMR showed recovery of systolic function, but persistent hypokinesia, myocardial edema, wall hypertrophy and T wave inversion remained.	Despite the lack of acute coronary process, thrombosis, or valvular displacement, The patient exhibited wall abnormalities directly attributed to tissue damage.	Viral cardiomyopathy is not the only route to cardiac wall damage outside of thrombosis or vascular issues. The mechanism behind myocardial injury in COVID-19 must be further understood. Myocardial inflammation in COVID-19 patients has been demonstrated, but long term effects remain to be understood.	**Weaknesses:** A single case report or myopathy with demonstration of occurrence by a yet to be understood mechanism. **Strengths:** Demonstration of myopathy other than viral prompts further examination into the mechanism of COVID-19 myopathies. The article has imaging available along with laboratory results and treatment plan. **Conclusion:** COVID-19 myopathies arise by other mechanisms than viral, coronary thrombosis, or valvular displacement, as evidenced by this case. Further exploration and examination is necessitated.

9. Bryant et al.	None	Retrospective Cohort Study	N = 3997	major Cardiovascular comorbidity, (DVT, PE, CVA,MI, AKI, Death) within 30 days after surgery	DVT or PE = both (1) (ICD-10) codes (I82 subset for DVT and I26 subset for PE) and (2) DVT or PE radiologic scan. CVA = both (1) CVA-specific imaging (noncontrast CT, head and neck CT, angiography, MRI, or magnetic resonance angiography) and (2) a postoperative neuro consult placement.MI = increase in the level of serum troponin of 0.04 ng/mL or more (to convert to micrograms per liter, multiply by 1.0). AKI = KDIGO criteria, extended to 30 days, rather than 7 days after surgery an increase in serum creatinine by 0.3 mg/dL or more (to convert to micromoles per liter, multiply by 88.4) within 48 hours or an increase in serum creatinine to 1.5 times baseline or more. For patients in whom a preoperative serum creatinine baseline was unknown, an estimated baseline value was inputted using the simplified Modification of Diet In Renal Disease formula based on age, sex, and ethnicity.	multivariable logistic regression	The median time from COVID-19 diagnosis to surgery was 98 days. 485 = major post op events (12.1%). Increased time from COVID-19 diagnosis to surgery was associated with a decreased rate of the composite Outcome. This trend persisted for the 1552 patients who had received at least 1 dose of COVID-19 vaccine.	**Weaknesses:** Single Center **Strengths:** Large sample size

11. Wollborg et al.	STROBE	Retrospective Study	n = Of 78,725 patients eligible for analysis, 11,004 COVID-19 negative patients were matched to 3,090 COVID-19 positive patients and 5005 pre-pandemic patients were matched to 2283 COVID-19 positive patients.	Presence of Afib or AFlutter	EKG, ECHO, Telemetry, other types of cardiac reports	Multivariable regression	COVID-19 positive patients had 1.19 times the odds (95% CI 1.00, 1.41) of developing AF compared to COVID-19 negative patients and 1.57 times the odds (95% CI 1.23, 2.00) of developing AF compared to pre-pandemic patients.	**Weakness:** **No Uniform AV detection (i.e. holter monitor)** **Strengths:**

Appendix E: Levels of Evidence Matrix

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Level I: Systematic Review or Meta-Analysis									✓					✓						
Level II: Randomized Controlled Trial			✓																	
Level III: Cohort Study		✓			✓		✓					✓								
Level IV: Case-Control Study																✓		✓	✓	
Level V: Quasi-Experimental Study																				
Level VI: Descriptive study																				
Level VII: Single-case experimental , case series								✓												
Level VIII: Expert opinion, background information, case report	✓			✓		✓				✓	✓		✓		✓		✓			✓

[1]American Society of Anesthesiologists [2]Bryant et al [3]Cohen et al [4]COVIDSurg Collaborative (2020) [5]COVIDSurg Collaborative, & GlobalSurg Collaborative (2021) [6]Hirata, N & Yamakage, M [7]Huang et al [8]Khalid et al [9]Mai et al [10]Mitrani et al [11]Nadim et al [12]O'Brien [13]Ong et al [14]O'Shaughnessy et al [15]Rohatgi et al [16]Sala et al [17]Sattar et al [18]Sivaloganathan et al [19]Wollborn et al [20]World Federation of Societies of Anaesthesiologist

Appendix F: EBP Nursing Research Committee Application

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

Name and Credentials: John Hintzman, BSN, RN, SRNA and Carolyn Olmsted, BSN, RN, SRNA
Unit: Surgery, Anesthesia
Email Address: colmsted@oakland.edu, johnhintzman@oakland.edu
Position and Unit worked at Beaumont Health: Oakland University-Beaumont Graduate Student Registered Nurse Anesthetist, Anesthesia
Site: Corewell Health William Beaumont University Hospital Royal Oak, MI
Evidence Based Project Title: Quality Improvement Analysis: Complications in Orthopedic Spine Patients with a History of COVID-19 Infection
Initial EBP Question: In adult orthopedic spine patients (P) how does adherence to surgical scheduling guidelines (I) affect the postoperative outcomes of length of stay, thromboembolic events, oxygen requirements, and arrhythmia (O) in patients with a positive history of SARS-CoV-2 compared to surgical patients without a COVID history (C)?

EBP Team Members: John Hintzman, Carolyn Olmsted, Dr. Lori Shannon, Dr. Anne Hranchook, Dr. Nicholas Gilpin, Rebecca Moody

Activities	
PRACTICE QUESTION:	
1. Define the problem	**Background:** Since the beginning of the SARS-COVID-19 pandemic in February 2020, vast changes have occurred in how operating rooms are managed and how surgical care is provided. At its start, COVID-19 infection caused many elective surgeries to be canceled, operating room schedules to be altered, and many hospital administrators and health care providers to search for best practices, valid information, and guidance on how to best care for surgical patients and those caring for them (COVIDSurg Collaborative, 2020). The desire to mitigate risk and promote health in the face of the pandemic is ever present. The primary target of COVID-19 is the pulmonary system; however, it is also known to cause endothelial dysfunction, vascular inflammation, and alterations in the coagulation cascade. Together these changes result in higher rates of deep vein thrombosis (DVT), pulmonary embolus (PE), and cerebrovascular accident (CVA) (Bryant et al., 2022). In addition, pulmonary complications, myocardial injury, and acute kidney injury (AKI) are thought to result from regional inflammation and cytokine release as a consequence of COVID-19 infection (Nadim MK, Forni LG, Mehta RL, et all, 2020). A study by the American College of Cardiology found that pulmonary edema secondary to viral myocarditis was found to be present in a significant number of otherwise healthy subjects after SARS-CoV-2 infection (Huang et al, 2020). The potential for COVID-19 to alter myocardial conduction, strength, and valvular function has significant implications to anesthesia care (Sattar, et al., 2020). Effective alveolar gas exchange has been shown to affect two major functional components: the integrity of alveolar epithelium and the patency and function of alveolar microcirculation. The inflammatory process that results from the infection activates the direct contact pathway for thrombosis formation (Wang et al., 2020). This presents the threat of venous thromboembolism and resultant pulmonary embolism. Taken together, these associations present a substantial potential mortality risk for surgical patients. Further, research has shown that undergoing anesthesia prematurely after recovery from COVID may present increased risk of postoperative complications and mortality (Deng et al., 2022). In an international cohort study published by the Lancet in 2020 authors write, "…Consideration should be given for postponing non-urgent procedures and promoting non-operative treatment to delay or avoid the need for surgery." Patients infected with COVID-19 scheduled for surgery within 6 weeks of infection are at an increased risk for morbidity and mortality (COVIDSurg Collaborative; GlobalSurg Collaborative, 2021). The Anesthesia Patient Safety Foundation (2021) submits that establishing the optimal timing of procedures for patients who have recovered from COVID-19 infection and the appropriate level of preoperative evaluation are challenging due to the lack of current evidence. Corewell Health William Beaumont University (CHE-WBUH) Hospital has developed surgical scheduling guidelines that indicate a timeline for when patients should be scheduled for surgery after testing positive for the COVID-19 virus. **Problem:** It has been identified that the CHE-WBUH Surgical Scheduling Guidelines (Appendix C) may not be consistently followed. Although multiple studies have examined the overall risk of mortality after COVID-19 diagnosis and surgery, the association of timing with morbidity and mortality warrants further investigation. The specific portion of the guideline to be evaluated relates to the amount of time surgery should be delayed after contracting Covid-19 and is as follows: **B. *CONSIDERATIONS FOR POST COVID-19 TIMING OF SUGERY TO MINIMIZE RISK OF POST OPERATIVE COMPLICATION*** **SCENARIO** | **WAIT TIME** | **SYMPTOMS**

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

	1	**4 Weeks**	Asymptomatic Pt. or Recovery from Mild, Non-Resp. Symptoms
	2	**6 Weeks**	Symptomatic (e.g. cough, dyspnea) Who **Did Not** Require Hospitalization
	3	**8 Weeks**	Symptomatic Pt. Who is Diabetic, Immunocompromised or Hospitalized and other co-morbidities
	4	**12 Weeks**	Required Intensive Care or Progressive Care Admission or prolonged (>48hrs ??) High Flow Oxygen therapy

Purpose of the EBP DNP Project: The purpose of this descriptive EBP-quality improvement DNP Project is to evaluate the time from COVID-19 diagnosis to surgery and expand on prior reports of perioperative outcomes after COVID-19 infection and to assess the risk of adverse outcomes including DVT, PE, CVA, myocardial injury, and pulmonary complications following surgery (COVIDSurg Collaborative 2020; COVIDSurg Collaborative - GlobalSurg Collaborative 2021; Bryant et al., 2022, ASA & APSF 2021). In addition, we will evaluate for variation in these associations based on patient vaccination status.

Project Aims:
1. The specific aim of this project is to retrospectively review postoperative outcomes of patients who underwent orthopedic spine surgery following a COVID-19 infection and evaluate timing of surgery with the postoperative outcomes listed.
2. A secondary aim is to evaluate overall compliance with scheduling of surgery using the CHE-WBUH Hospital Surgical Scheduling Guidelines following COVID-19 infection.

2. State the EBP question	In adult orthopedic spine patients diagnosed with COVID-19 infection (P) how does time to surgery (I-1) and compliance with CHE-WBUH Surgical Scheduling Guideline (I-2) impact the risk of major postoperative morbidity (O) in the immediate postoperative period (T)?
3. Identify stakeholders (who will be impacted – i.e., patients, members of the multidisciplinary team, etc....	**Stakeholders include:** Orthopedic spine patients Dr. Nicholas Gilpin – Director of Epidemiology Rebecca Moody, MS, CRNA – Senior Director-Surgical Services CHE-WBUH orthopedic spine surgeons CHE-WBUH nurses and other healthcare members of the interdisciplinary team
EVIDENCE:	
4. Conduct internal and external search for evidence (provide summary of the evidence and reference list)	Sequelae ranging from "COVID-19 Long Hauler" syndrome to the development of severe myocarditis have been described after COVID-19 infection (Sattar et al., 2020). The potential of increased hemodynamic instability during anesthetic administration, decreased respiratory efficiency, and cardiovascular changes secondary to COVID infection presents the need for a formal analysis of health literature. Maintenance of evidence-based anesthesia practice is imperative for providing safe patient outcomes, especially amidst a continued pandemic. Exploration of the physiologic changes following COVID -19 infection and timing of surgery is described in the literature and supports conducting a retrospective chart review to answer to answer the PICOT question. In order to facilitate the evaluation of timing of surgery and compliance with the CHE-WBUH Surgical Scheduling Guideline on postoperative outcomes for patients diagnosed with COVID-19 infection, a singular surgical population was selected. The adult orthopedic spine population was selected as these surgeries are often elective, are typically performed at equal rates in men and women, and generally exclude patients that are morbidly obese. **Internal Evidence:** A Surgical Scheduling Guideline was developed by Dr. Gilpin in epidemiology in response to inquiries from physician anesthesiologists after several articles were published around recommendations. Observation on the part of anesthesia and nursing indicates that there is variability in the application of how this guideline is applied. Given the knowledge gleaned from the literature review, timing of surgery following COVID-19 infection is important in preventing morbidity. **Literature Review Method** A literature review for COVID related long term sequelae was performed using the following databases: CINAHL complete (Cumulative Index to Nursing and Allied Health Literature) through EBSCO host, Cochrane Library, PubMed, and Google Scholar. Given that COVID-19 is a recent occurrence, only relevant articles published between November 2020 and December 2022 were included. Specific search terms used included: "COVID-19", "coronavirus", "long term", "respiratory", "pulmonary", "lungs", "myocarditis",

"cardiomyopathy", "surgery", "anesthesia", "arrhythmia", and "adverse events". Keyword search included "anesthesia AND COVID-19 OR coronavirus", "COVID-19 OR coronavirus AND surgery AND outcomes", "COVID-19 AND cardiomyopathy", COVID-19 AND respiratory" "orthopedic spine", "surgery", "postoperative complications", and "adverse events". Keyword search included "orthopedic spine AND postoperative complications", "orthopedic spine surgery AND adverse events", "orthopedic spine complications".

Inclusion criteria included the surgical setting in all or part of data sets. Exclusion of pediatric patients, ICU patients, ventilated patients, critically comorbid patients, trauma patients, and unknown histories were maintained for consistent validity. Due to the recent and still developing nature of COVID-19 and its effects on healthcare, both experimental and non-experimental studies were included for this review in order to gain knowledge and form a general consensus and understanding. Empirical literature, controlled trials, experimental studies, and case reports were included to view the problem at hand from various lenses.

Respiratory Sequelae

When examining the effect which COVID-19 has had, it is difficult to ignore the profound respiratory complications with which this virus is associated. Supplemental oxygen dependency, increased ventilatory requirements, and hospital shortages of ventilators and ICU rooms and staff are topics which have become commonplace among the public due to COVID-19's profound impact on the respiratory system. Despite all these respiratory complications, research exploring the long-term respiratory effects of the virus is still emerging; of all COVID-19's long term physiologic impact, pulmonary complications are the most prevalent. Similar to previous SARS infections, of which COVID-19 is related, the virus causes intra-alveolar thrombosis and airway inflammatory viral damage which contribute to the development of fibrotic changes in the pulmonary system (Wang, et al., 2020).

One of the newly established methods of COVID-19 access to the intracellular systems of the body is via the angiotensin-converting enzyme 2 (ACE2) receptor on relevant cell surfaces. "Many factors have been associated with both altered ACE2 expression and COVID-19 severity and progression, including age, sex, ethnicity, medication, and several co-morbidities, such as cardiovascular disease and metabolic syndrome" (Bourgonje, et al., 2020). These receptors are highly prevalent in pulmonary tissues. This is where the body converts angiotensin I to angiotensin II in the Renin-Angiotensin system and where the ACE2 receptor is known to regulate other byproducts of the conversion including variables of bradykinin, ghrelin, and many more. It is the proliferation of these receptors, not necessarily their function which is exploited by the COVID-19 virus as the virus structure has a certain affinity for the receptor. This affinity allows for the proliferation of the virus in a multitude of body tissues (Shang, et al., 2020). Bourgonje et al. (2020), explain: "ACE2 [is] highly expressed on lung alveolar epithelial cells and small intestinal epithelial cells, consistent with potential routes of viral transmission of [COVID-19]. [ACE2] is present on vascular endothelial cells and smooth muscle cells in all organs studied … ACE2-expressing organs do not equally participate in COVID-19 pathophysiology, implying that other mechanisms are involved in orchestrating cellular infection resulting in tissue damage".

Within the pulmonary tissues, COVID-19 has also been found to attack type 2 pneumocytes directly by binding to the cell surface and destroying them through viral multiplication and reproduction (Wang, et al., 2020). The combination of these two proliferation methods causes profound damage within the pulmonary tissues, which are now being attributed to longer-lasting long-term sequelae of the virus. A relationship between the severity of the viral infection and severity of lung damage has been established (Wang, et al., 2020). According to Wang et al., "The virus can injure the lungs in 3 ways: acute respiratory distress syndrome (ARDS) with diffuse alveolar damage (DAD), diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation. The results of these combined actions include impaired alveolar oxygenation, hypoxemia, and acidosis." These processes then lead to "extensive diffuse alveolar damage with bilateral oedema, proteinaceous or fibrin alveolar exudates, and diffuse reactive hyperplasia of type II pneumocytes consistent with fibrosis" as described by Bourgonje, et al. (2020). In essence, pulmonary changes resulting from COVID-19 infection may initially present as pneumonia, but the acute lung damage caused may result in chronic impairment of lung function and possibly pulmonary fibrosis, both of which result in impaired quality of life. These changes in pulmonary function "can have profound effects on daily quality of life for people initially believed to have recovered from COVID-19" (Wang et al., 2020). Given these substantial and long physiologic changes brought on by COVID-19, there is the possibility of unforeseen complications in surgical patients undergoing anesthesia who are believed to have fully recovered from COVID-19.

COVID-19 Associated Myocarditis

An article written by Hirata & Vavalaga (2020) titled *Cardiovascular Considerations for Anesthesiologists During the COVID-19 Pandemic* covers multiple avenues of COVID-19 specific cardiac complications which concerns the anesthesiologist outside of typical airway and ventilatory management. The authors gathered emerging data to highlight important perioperative cardiovascular considerations associated with COVID-19 infection. They found a high incidence of myocardial injury and cardiomyopathy in patients with severe COVID-19 ranging from 7.2-27.8%. These injuries and abnormalities range from left ventricular dysfunction, persistent hypotension, myopericarditis, myocarditis, arrhythmia, and heart failure. They suggested several

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

mechanisms of injury such as direct viral invasion, systemic inflammatory responses, coagulation disruptions, and pneumonia induced hypoxia as contributing or causative factors stemming from myocarditis. A parallel between severe sepsis induced myocardial complications caused by excessive inflammatory response and COVID-19 infection was drawn, citing the elevation of proinflammatory cytokines, and hypercoagulable state with both disease processes. A suggested mechanism of COVID-19 cardiac and pulmonary cell infection by way of ACE2 receptor infiltration was proposed based on ongoing research, attributing myocardial and lung injury to direct viral infiltration within the cell (Cohen et al., 2020). The authors state anesthetic concerns with the COVID-19 patient include exacerbated inflammatory responses during surgery and intensified cardiovascular disease processes which increase morbidity and mortality with increased cardiac risk factors such as hypertension, diabetes, hyperlipidemia, atherosclerosis, and advanced age. Finally, the authors propose that vigilant monitoring of cardiac status is warranted with COVID-19 patients due to their increased cardiac risk status, and there is further research needed to improve perioperative management of COVID-19 patients (Hirata & Vavalaga, 2020).

Given the ACE2 receptor theory of cardiac tissue infiltration of the COVID-19 virus, several studies have found myocarditis to be prevalent among those who have had a COVID-19 infection. A study done by Huang, et al (2020) found evidence of persistent cardiac disease in patients recovered from COVID-19. Their purpose was to evaluate the presence of cardiac involvement in patients recovered from COVID-19 using cardiac magnetic resonance imaging (CMR). A single center retrospective observational study of 26 patients recovered from COVID-19 who reported cardiac symptoms were retrospectively studied. These patients did not have baseline studies done prior to infection. Of the 26 patients, 15 were found to have abnormal CMR findings including myocardial edema in 14 patients, and 8 patients presented with late gadolinium enhancement which predicts adverse cardiovascular outcomes in patients with nonischemic cardiomyopathy. These patients were also found to have decreased right ventricular function. The researchers conclude that due to abnormal CMR findings compared to traditional acute viral myocarditis, the results suggest the existence of diffuse myocardial edema and fibrosis specific to COVID-19 infection. The major weakness of this study revolves around the small sample size with non-random sampling of patients, and the majority of patients exhibiting moderate COVID-19 infections which may be non-reflective of severe and critical infections. As such the researchers admit their results cannot be extrapolated to a larger population, however this study demonstrates the phenomenon of post-COVID-19 cardiac involvement and can be used to inspire further research (Huang, et al., 2020).

A systematic review of abnormal cardiovascular magnetic resonance findings in recovered COVID-19 patients was performed by Kim, Han & Suh (2021). This review included 890 patients from 16 studies. All CMR scans were performed within 22 weeks of COVID-19 recovery. The researchers found abnormal CMR findings in recovered COVID-19 patients to be 46.4%, with explicit myocarditis and late gadolinium enhancement in 14% and 20.5% of cases respectively. Through retrospective analysis, the researchers found that athletes specifically and patients with normal cardiac enzyme levels had a lower prevalence of abnormal CMR findings. Various limitations identified by the researchers due to small sample and subgroup sizes included lack of sufficient subgroup analysis, and limited analysis of ventricular systolic dysfunction. The researchers also cited a lack of certain data necessary for subgroup analysis such as presence of specific cardiac symptoms, underlying cardiac disease, and ECG or echo abnormalities. Lastly, the need for longer-term studies is necessary to determine clinical significance of these findings is established by the authors (Kim, Han, & Suh, 2021).

COVID-19 Induced Arrhythmia

A systematic review and meta-analysis by Garcia-Sevora et al (2020) sought to estimate the presence of ECG abnormality and cardiac arrhythmia in hospitalized patients with COVID-19 infection. Additionally, association of arrhythmia with patient outcomes were made. Results from the review and analysis of 30 studies show that supraventricular tachycardias, ventricular tachycardias, QT prolongation, ST segment deviation were the most common arrhythmias in patients with COVID-19 infection. Associated outcomes with arrythmia included mechanical ventilation, development of further arrhythmia, worse prognosis, and increased mortality. Limitations to this study were unreported type of arrhythmia in half of the included studies. Without specificity for the type of arrhythmia found, practical application to the clinical anesthetic setting is limited. Additionally, the review did not include assessment of long-term outcomes of COVID survivors which makes a direct connection to subsequent anesthesia-based research less likely. However, it being the largest meta-analysis surveying ECG changes in COVID-19 patients provides a valuable starting point for future inquiry.

A review paper by the American Journal of Medicine pertains directly to the newly observed phenomenon of cardiac arrhythmia present during Post-Covid Syndrome. Stalberg et al., (2021) write, "Given the extremely high number of reported cases and the uncertain long-term prognosis, post-acute COVID-19 syndrome is likely to become a major clinical problem for the foreseeable future." They note increased frequency of abnormal sinus tachycardia and premature ventricular contractions in COVID-19 survivors and suggest a post-covid tachycardia syndrome be considered a subsyndrome of post-acute COVID-19. While the paper does not include statistical backing of its claims, it does provide another foundation for further research relating to anesthesia care. Treating post COVID-19 arrhythmias as a novel clinical syndrome and performing interventional studies and testing of established and novel pharmacological approaches highlights again, the purpose of subsequent research.

Another review article by Sattar et al (2021) provides a concise description of the pathophysiology and treatment of the cardiac sequelae of COVID-19 infection. They summarize the cardiac impact of COVID-19 on the cardiovascular system as evidenced through multiple studies which report myocarditis in 7–17%, heart failure in 24%, arrhythmias in 17% and thrombotic complications in 31% of hospitalized COVID-19 cases. This provides further support for future research on this topic. Again, this article is limited in that it lacks statistical methods to demonstrate significance and effect; however, it remains a useful piece of literature to include in this review as it demonstrates the need for prevention and treatment of cardiac sequelae to limit morbidity and mortality for our patients (Sattar et al., 2020).

Neurological Sequelae

As COVID-19 has already been studied as invading almost every tissue within the body, brain tissue is no exception. "Increasing reports have shown that [COVID-19] infection involves the central nervous system and the peripheral nervous system and directly or indirectly damages neurons, leading to long-term neurological sequelae" (Wang, et al., 2020). Covid Long-Hauler syndrome described as prolonged brain fog and difficulties in cognition has been described by numerous studies since 2020 (Sattar et al., 2020). Cognitive changes including but not limited to anxiety, depression, insomnia, memory loss and cognitive changes have been previously described one year after covid infection (Han, et al., 2022). Even in a qualitative study of one year post covid patients, some degree of motor impairment has been observed in 25.8% of subjects (Bellan, et al., 2022). Wang, et al., (2020) describes the physiology of COVID-19's invasion into neuronal tissues in three distinct ways. First, the widely established ACE2 receptor is widely expressed in brain vascular endothelial cells, allowing COVID-19 access to cells which control the brain's blood supply. Second, the invading S protein of the COVID-19 virus can directly damage the integrity of the blood brain barrier to varying degrees. Third, Wang et al., (2020) relate how the virus can induce the inflammatory response of the microvascular endothelial cells that change the function of the blood brain barrier. As previous studies have mentioned, neurological symptoms as described in Covid Long-Hauler syndrome and cognitive impairment and memory loss are prevalent among recovered COVID-19 patients. The physiology of COVID-19s invasion into neuronal tissue is widely described and cannot be ignored, especially given the widespread expression of ACE2 receptor sites throughout the body. This means that COVID-19 can alter the blood brain barrier and enter the brain, supporting the appearance of neurological symptoms, the formation of fatal microthrombi, and the occurrence of encephalitis induced by COVID-19 (Wang, et al., 2020).

Thromboembolic Events

A current hot topic among news headlines is the occurrence of blood clots in COVID-19 patients as well as those who have received the vaccine. Current literature does not appear to have a clear consensus on the long-term thrombotic sequelae of previous COVID-19 infection. Although well documented in acute COVID-19 infection, due to the release of cytokines and rampant bradykinin releases, "patients are at particular risk for developing coagulopathy reminiscent of disseminated intravascular coagulation (DIC) which was associated with mortality, possibly due to both venous and arterial thrombosis" (Bourgonje, et al., 2020). The authors go on to describe how due to COVID-19's affinity and prevalence of ACE2 receptors, and it's role in bradykinin and other endothelial mediators, circulating biomarkers of endothelial activation, which could include increased susceptibility to blood clot formation, have been reported in recent studies (Bourgonje, et al., 2020).

Postoperative Outcomes of Orthopedic Surgery

In the immediate postoperative period, several complications have been reported in the academic literature. Complications related to anesthetic care, patient positioning, and surgical technique have been excluded from this literature review to focus on the relationship between postoperative complications and systemic effects of COVID-19 infection specifically. Postoperative complications of orthopedic spine surgery can be severe and can lead to permanent morbidity if left unrecognized and untreated (Swann et al., 2016).

In a review by the University of Texas Southwestern Medical Center, the following unmodifiable postoperative complications have been identified from orthopedic spine surgery: Myocardial Infarction 1-2%, Stroke 0.014% - 0.20%, Hemorrhage >3L ~3.0%, Respiratory & Pulmonary Complications ~13%, Pulmonary Embolism 0.3 to 1.4%, Pulmonary Edema 1.3%, and coagulopathy as defined by international normalized ratio (INR) > 2, platelets <50, or fibrinogen <100 0.82% (Swann et al., 2016). These benchmarks can serve as a comparison to postoperative outcomes in patients with a positive COVID history.

Scheduling of Surgery After COVID-19

An emerging area of study is concerned with the timing of surgery in relation to a patient's COVID-19 infection. Yanis et al (2021) note that is imperative for health care providers to clearly convey the risks associated with each procedure while also acknowledging that other factors such as COVID 19 infection may also alter the patient's the risk profile. In a study by the British Journal of Surgery in 2020, authors identified that more research is needed to verify guidelines that will offer clinical benefit and the optimal length of time for delaying surgery in patients with COVID-19 infection.

A study published in the journal "*Annals of Surgery*" (2020) helps to stratify the timing of infection in relation

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

to postop complications. Authors conclude that major elective surgery scheduled 0 to 4 weeks after SARS-CoV-2 infection is associated with an increased risk of postoperative complications. Surgery performed 4 to 8 weeks after SARS-CoV-2 infection is still associated with an increased risk of postoperative pneumonia, whereas surgery scheduled 8 weeks after Covid-19 diagnosis is not associated with increased complications. The American Society of Anesthesiologist and the Anesthesia Patient Safety Foundation (2021) have recently published updated guidelines advocating for waiting ≥ 7 weeks to schedule elective surgery for unvaccinated patients and to weigh the risks of the procedure against time sensitive needs in all patients. A multi-country study (116) and multi-center study (COVIDSurg Collaborative, 2021) followed more than 140,000 patients with 3, 127 having a COVID-19 infection demonstrating a 30 day mortality of 3.09 (CI 1.64-4.54) for patients having surgery 0-2 weeks following infection and a continual decline in risk to 0.64 (CI 0.20 – 1.07) ≥ 7 weeks following infection. The risk for patients without a COVID-19 infection was similar to waiting ≥ 7 weeks and was 0.62 (CI 0.57-0.67).

Conclusion

After an extensive review of the literature pertaining to the complexities surrounding the sequelae of COVID 19 on survivors, several conclusions and limitations have been established. One aspect that is clear is that data and information related to this issue is very much developing. Further, the volume of cases related to the desired research area with adequate follow up for long term study is low, hindering the ability to identify distinct practice guidelines at this time. More specific research over the next few years will be necessary to establish practice guidelines for surgical scheduling that allow safe administration of an anesthetic to patients who are in the early stages of recovering from COVID-19. This review of the literature supports a quality improvement initiative to assess surgical scheduling guidelines and outcomes for patients who are post COVID 19 infection scheduled for surgery.

TRANSLATION:

5. Describe action plan, and assessment of any/all safety risks. Provide copy of any survey or data collection tool.

Include Insurance of confidentiality – Data Use Agreement for any external data dissemination, identification of site, system, staff, patients, etc. DUA can be started by contacting the Research Institute Manager at Bobbie.Lewis@beaumont.org

This project will be completed using the "Plan Do Study Act" model which is a straightforward, iterative approach to quality improvement. The model is depicted in the graphic below:

Plan:

Improvement goal: To answer the PICOT question by examining the association between time to surgery after COVID-19 diagnosis and the incidence of major postoperative morbidity events for patients undergoing orthopedic spine surgery at CHE-WBUH hospital. Using the data collected, 1. determine if changes to the current CHE-WBUH hospital surgical scheduling guideline is needed 2. determine if education is needed to improve compliance 3. develop recommendations based on findings.

Predict what will happen: Patients that are scheduled for surgery earlier than the recommendations of the CHE-WBUH Surgical Scheduling Guideline for patients post COVID 19 infection will demonstrate morbidity and mortality consistent with findings in the literature.

Plan the cycle:

- **1. WHO**: Develop the interprofessional team: In June of 2022, DNP Students (John Hinzman, RN, BSN, SRNA & Carolyn Olmsted, RN, BSN, SRNA) met with Corewell Health William Beaumont University physician and epidemiologist (Dr. Nicholas Gilpin) & the Senior Director of

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

	Surgical Services (Rebecca Moody, MS, CRNA) to confirm the Surgical Scheduling Guideline policy and obtain support to conduct a quality improvement project looking at patients following COVID 19 infection, surgical scheduling timeline following infection and postoperative outcomes. - **The stakeholders are**: - Patients - Epidemiology - Surgeons - Nurses - Administration - **2. WHAT DATA:** - **Inclusion criteria include the following:** - adults 18 years or older - history of undergoing orthopedic spine surgery between January 1, ~~2021~~ and June 30, 2021 at CHE-WBUH hospital - history of testing positive for COVID as documented by a positive polymerase chain reaction (PCR) test result within 8 weeks of ~~surgery~~ - - **Exclusion criteria ~~includes~~** - age less than 18 years - non orthopedic spine surgical patients having surgery at CHE-WBUH - patients not testing positive for COVID as documented by a positive polymerase chain reaction (PCR) test result within 8 weeks of ~~surgery~~ - **Data to be collected:** Upon approval from the Beaumont Nursing Inquiry, EBP, Research Council to conduct this QI project, the team will review charts that meet that following inclusion criteria: *Outcome Variables:* - Deep Vein Thrombosis (DVT) - Pulmonary embolism (PE) - Cerebral Vascular Accident (CVA) - Myocardial Injury (MI) - New onset arrythmia - Death - Postoperative pulmonary complications: - Pneumonia - ARDS - Unexpected postoperative ventilation. - - *Population Variables* - Age – categorically collected to protect patient ~~identity~~ - Sex - BMI - ASA Classification - Postoperative length of stay - Grade of surgery: minor, major - Urgency of surgery: elective, emergency - Time from diagnosis of SARS COV-2 ~~to day~~ of surgery - Vaccination status for COVID - - - **3. WHERE**: Corewell Health William Beaumont University Hospital - **4. HOW:** The proposed DNP project is a retrospective chart review assessing the above outcome variables. Data will be collected from Epic ® Electronic Health Record, data analysis will follow, and a presentation of the findings will be created and shared with CHE-WBUH and Oakland University Beaumont DNP-NA Students & Faculty. Data analysis will be conducted using SPSS. - **Data collection tool**: See Appendix A **Definitions:** See appendix B **CHE-WBUH Surgical Scheduling Considerations after Covid 19**: Appendix C

Nursing Evidence-Based Practice, Quality Application
Beaumont Nursing Inquiry, EBP, Research Council

	-
6. Disseminate findings. - describe your plan for dissemination of the results of your project (at Beaumont and externally)	Findings will be presented at the Oakland University- Beaumont DNP-NA Dissemination Day. In addition, the findings will be presented to Dr. Gilpin and the anesthesia department at CHE-WBUH hospital. The presentation will include a verbal overview, visual aids (PowerPoint), and time for interactive discussion. The leadership team will collectively prepare an abstract and poster to be presented at the organization's quality improvement conference.

Manager/Director or CNO approval: _____

Appendix G: Nursing Research Committee Approval Letter

Corewell Health East

Nursing EBP, Quality and Research Council

Nursing Evidence Based Practice Application Review
Date: March 23, 2023
To: John Hintzman BSN, RN, SRNA and Carolyn Olmsted BSN, RN, SRNA and Lori Shannon (Faculty)
RE: Quality Improvement Analysis: Complications in Orthopedic Spine Patients with a History of Covid 19 Infection

Dear John and Carolyn and Lori,

Your Quality Improvement application was reviewed by the Beaumont Health Nursing Evidence Based Practice, Quality and Research Council. This council consists of site representatives from all of our sites – including Directors of Education and Research, CNO's, Research Institute Managers, and various leaders from Corewell Health East. Thank you for participating in the Council review process! It was very informative and is a great project.

The following comments were discussed:

- Data Attestation Agreement is needed – attached to your email
- If you need assistance in the data collection process, please let us know and we can reach out to our quality department
- Suggestion to change time frame to 12 weeks

The Council has approved your EBP application. Please save this Outcome Letter for your records. Please return the Data Attestation form at your earliest convenience.

Please let me know if you have any additional questions. On behalf of the Corewell Health East Nursing EBP Quality and Research Council, good luck with your project!

Andrea Carr

Andrea Carr DNP, MSN, MSA, RN, NEA-BC
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Chairperson- Nursing EBP, Quality and Research Council
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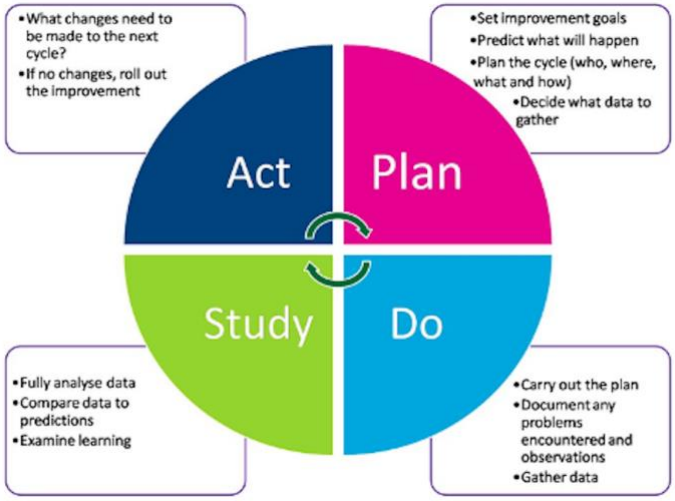
Appendix H: Plan-Do-Study-Act Model



Appendix I: Donabedian Theoretical Framework Model