Spring 4-28-2024

Development and Implementation of an Evidence Based Practice Guideline Related to the Management of Adult Angioedema

Megan Przybysz
Otterbein University, meganprz@gmail.com

Final Scholarly Project: Development and Implementation of an Evidence Based Practice Guideline Related to the Management of Adult Angioedema

Megan Przybysz, BSN, RN

Department of Nursing, Otterbein University

2023

In Partial Fulfillment of the Requirements for the

Degree Doctor of Nursing Practice

DNP Final Scholarly Project Team:

Dr. Brian Garrett, DNP, CRNA, Project Team Leader

Dr. Chai Sribanditmongkol, PhD, RN, IBCLC, CNS, Project Team Member

Dr. Amy Bishop, DNP, AGCNS, Project Team Member

Abstract

Angioedema (AE) is a potentially life-threatening medical condition that occurs with a higher frequency than medical providers may expect, with the emergency department (ED) serving as the usual first point of medical contact for patients. Any hesitation in recognizing AE or inconsideration of the disease process in differential diagnoses may lead to a dangerous delay of care. Due to the potential rapid progression of airway obstruction in AE, inexperienced providers should not attempt intubation, instead deferring to providers experienced in alternative airway techniques (i.e., anesthesia providers). The primary goal of this project is to develop an evidence-based practice guideline for AE to facilitate a quality improvement project for guideline implementation. The proposed guideline offers medication choices for AE patients, steps for providers to follow when presented with an AE case, and suggests intubation and emergency surgical airway techniques. Project implementation involves retrospective and prospective chart reviews, in person staff training, and the creation of an angioedema cart containing all necessary medications and intubation supplies suggested in the guideline. The project also supplies an infographic algorithm for quick use, with separate task lists for ED and anesthesia providers. If implemented, the full proposed timeline for training and data gathering would be one year, with the outcomes of patient mortality, hypoxic brain injury, cardiac arrest, and airway placement metrics to be assessed via chart review pre and post guideline implementation. The project emphasizes the importance of successfully managing AE and the guideline hopes to serve as a quick resource to providers dealing with emergent AE airway issues.

Keywords: Angioedema, guideline, anesthesia, emergency room, emergency department, difficult airway team, airway management, angioedema protocol/guideline/procedure/policy

Development and Implementation of an Evidence Based Practice Guideline Related to the Management of Adult Angioedema

Angioedema (AE) presents as a sudden onset of non-pitting edema to the skin and mucous membranes with two main forms, mast cell mediated and bradykinin-induced (Misra et al., 2016). In mast cell mediated AE, the body releases immunoglobulin E (IgE) in response to an irritant, leading to the degranulation of mast cells (Misra et al., 2016). Anaphylaxis is the most severe form of mast cell mediated AE (Misra et al., 2016). The second type of AE is triggered by either the overproduction of bradykinin or the prevention of bradykinin breakdown (Misra et al., 2016). Mast cell activation typically does not occur in bradykinin induced AE, with edema instead due to increased vascular permeability (Misra et al., 2016). Angiotensin-converting enzyme inhibitors (ACEi) AE is the most common type of bradykinin induced AE (Misra et al., 2016). Calcium channel blockers, propofol and non-depolarizing neuromuscular blockers (particularly rocuronium) are additional noted triggers for bradykinin induced AE (Misra et al., 2016).

According to the World Allergy Association, AE may affect up to 20% of the world's population (Misra et al., 2016). In the United States, up to 25% of individuals may experience AE or urticaria at some point, with over one million of those cases leading to an emergency department (ED) visits each year (Bernstein et al., 2017). Of the one million ED visits for AE annually, up to 30% are related to ACEi (Bernstein et al., 2017). ACEi consumption leads to an increased risk of AE, where up to 2.5 % of individuals taking an ACEi experiencing AE, with an especially elevated risk for African Americans (Misra et al., 2016). Due to better availability and cost effectiveness of ACEi, the medical community reports an increase in the number of ACEi prescriptions, contributing to an increased number of AE ED visits (Misra et. el., 2016).

Likewise, hospital admissions due to AE increased from 29.3 in 2006 to 35.8 per 100,000 in 2010 (Misra et al., 2016; Pandian et al., 2019). In one survey, 91% of patients with hereditary AE (HAE) reported more than one lifetime ED visit for AE, with 33% reporting a visit within the last year (Otani et al., 2017). Increased ED visits and hospitalizations leads to increased total spending on AE. Total AE spending per patient is approximately $96,000 per year, with hospital costs attributing the majority of that sum, at 68% (Otani et al., 2017). Additionally, delayed interventions and the necessity of surgical airways from inconsistent AE management increases the cost to both the facility and the patient, as the patient requires a longer in house, often intensive care unit, admission (Misra et al., 2016).

Studies estimate that up to 34% of patients presenting to the ED for AE require intubation, which creates a challenge for providers due to the complexity of establishing an AE airway, secondary to swelling and changes to airway anatomy (Pandian et al., 2019; Driver & McGill, 2017). In a difficult airway situation, the first airway placement attempt is the best chance for success at establishing the least invasive airway (Rosi-Schumacher et al., 2020). The AE airway is sensitive to manipulation, which potentially triggers worsening airway obstruction (Rosi-Schumacher et al., 2020). Due to the increased sensitivity of an AE airway, any attempts at airway manipulation should be reserved for experienced providers.

According to Driver and McGill (2017), of those who do require airway interventions, between 8 and 33% require surgical airways. Not surprisingly, due to the difficulty in placing an AE airway, a review of the National Emergency Airway Registry shows ED providers successfully placed AE airways on first attempt in only 81% of occurrences (Sandefur et al., 2021). A 19% first pass failure rate is high considering the stakes, suggesting that an alternative process is necessary, supporting the need for the introduction of an AE guideline.

Significance to Anesthesia

The World Health Organization (WHO) and the World Allergy Association (WAO) current recommendations push for early, aggressive airway management techniques in AE, either with intubation or surgical methods (Vuzutas & Sarafoleanu, 2016; Maurer et al., 2018). With difficult airway management being one of the defining realms of anesthesia providers, emergency department (ED) and intensive care unit (ICU) providers rely on anesthesia for airway assistance (Cook & MacDougall-Davis, 2012). However, the request for assistance often occurs as a "second phase response" (Gonzalez et al., 2016, p. 194). In a second phase response, providers do not request assistance until after previous unsuccessful attempts to secure the airway, leading to delay in obtaining a definitive airway (Gonzalez et al., 2016).

Securing the AE airway presents challenges to any provider, as success often requires the utilization of alternative intubation methods, such as fiberoptic bronchoscopes (FOB), video laryngoscopy (VL) or nasal intubation (NI; Parkey et al., 2019). As the "airway experts," anesthesia providers may have increased access and familiarity with these alternative intubation techniques (Parkey et al., 2019). The anesthesia and otolaryngologic communities traditionally held the belief that awake intubation via FOB was the gold standard for difficult intubations (Vuzutas & Sarafoleanu, 2016). However, AE airway edema can lead to the inability to intubate despite alternative methods and necessitate surgical airway placement (Vuzutas & Sarafoleanu, 2016).

As previously mentioned, between 8 and 33% of AE patients needing airway intervention require a surgical airway (Driver & McGill, 2017). In a worst-case scenario, airway edema from AE may result in a "cannot intubate, cannot ventilate" (CICV) situation, necessitating the initiation of a surgical airway. Although CICV situations are rare, up to 25% of anesthesia

related deaths occur due to the inability to ventilate the patient (Cook & MacDougall-Davis, 2012). Additionally, airway events that happen outside of the operating room (OR) lead to higher rates of patient harm, with death or brain damage 38-fold higher in events occurring in the ED and 58-fold higher in the ICU compared to the OR (Cook & MacDougall-Davis, 2012). The increased rates of patient morbidity and mortality in an out of OR environment stress the importance of increased anesthesia provider vigilance and training to improve patient safety (Cook & MacDougall-Davis, 2012).

Although the medical community considers anesthesia providers to be an expert resource in difficult airway management, literature shows that anesthesia providers have a lack of AE training, lack of opportunity to practice difficult airway skills, including alternative airway techniques, and a lack of immediate access to equipment, medications, and supplies (Popovici & Mitre, 2018; Heard et al., 2009; Bernstein et al., 2017)**.** In a case-controlled study at Johns Hopkins, Pandian et al. (2019) showed that the implementation of a specific AE management protocol, with step-by-step instructions, can combat delays in care and misdiagnosis. Additionally, Pandian et al. (2012) found that the implementation of an AE program increased the time available for appropriate airway evaluations prior to intervention and decreased the attempts needed to obtain definitive airway placement. Research from Javaud et al. (2015) supports the findings from the Johns Hopkins study, proposing that an organized approach to AE not only leads to speedier interventions, but also faster relief of AE symptoms.

Project Objectives

The primary intention of this project is the creation of an evidence-based practice (EBP) guideline for the management of AE through a quality improvement (QI) project, with suggestions for implementation and outcome tracking. According to the United States

Department of Health and Human Services Health Resources and Services Administration (HRSA; 2011), successful QI project implementation leads to improved quality, efficiency, and profitability. To develop an AE guideline, the project will apply the following objectives:

- conduct a thorough literature review and synthesis of AE management, including medication selection, intubation techniques, difficult airway equipment, and historical implementation of AE guidelines by other facilities,
- development of a comprehensive EBP guideline for AE management, guided by the completed literature review,
- development of a comprehensive implementation plan for the created guideline, encompassing costs, supplies, stakeholders, staff training, and timelines, and the
- development of a project evaluation plan, including tracked outcome indicators, frequency and methods of monitoring, anticipated outcomes, and potential interventions for further project implementation or modification.

Project Framework Model

The current project employs Duke University‘s FADE model (Focus, Analyze, Develop, and Execute/Evaluate) as the structure for project development, implementation, and analysis (Appendix A & B; BHM, n.d). The FADE model provides guidance in how to effectively implement an EBP AE guideline. Focus stresses the importance of project selection; defining a specific, relevant problem to assess (BHM, n.d). Completion of a literature review shows having a delineated AE guideline in place works to reduce morbidity and mortality related to AE. Although the intended project hospital has a difficult airway team in place, the facility does not currently utilize a guideline for AE management, which results in varying methodologies for both medical management and airway establishment.

A retrospective chart review at the proposed hospital showed a delay in establishing a definitive airway in AE patients, resulting in episodes of patient harm. Anesthesia department meetings and informal discussions with anesthesia leadership at the proposed project hospital led to the identification of potential reasons for delayed care and invasive airway interventions. Anesthesia department representatives believe ED providers have less emergent airway experience, due to the presence of newer providers/residents, and do not call for airway assistance until after the patient is experiencing symptoms of respiratory distress. The project goal is to determine if the implementation of a hospital wide guideline for AE assists with guiding best practice management of a potentially life-threatening situation. Drafting of the PICOT question is the culmination of the "Focus" step of the FADE model, serving as a concise summary of an identified problem at the project facility (BHM, n.d.).

After defining the problem, the next step in the FADE model is "Analyze," which consists of collecting and analyzing baseline data and determining influential factors (BHM, n.d.). To complete this phase, the project team will complete a retrospective chart review of the following: the number of AE cases, the number of AE cases needing airway intervention, the time from patient arrival to placement of definitive airway, the number of attempts to successful airway placement, and the number of surgical airways. Additionally, the project team will look at the number of AE cases resulting in patient mortality, hypoxic brain injury, and cardiac arrest. The project team selected the datapoints for assessment to align with datapoints selected by researchers in the literature (Alvis et al., 2016; Biro & Schlaepfer, 2018; Darby et al., 2019; Cook & MacDougall-Davis, 2012)

The final sections of the project will focus on the "Develop" and "Execute" sections of the FADE model (BHM, n.d.). Based on information obtained in the literature review and the

facility needs assessment, the “Develop” section will discuss the development and proposed implementation plan for an AE guideline, the timeline for guideline implementation, budget, and associated trainings. The “Execute” section of the project will discuss stakeholder approval needed for implementation, the plan for implementation, methods to monitor guideline success, and potential modifications to the guideline if the project does not meet intended objectives.

Focus

Problem Selection (PICOT Question)

A PICOT question serves as a planning and structural guide for nursing projects. A PICOT question should address the following components: identification of a target population, a baseline dataset and a specific intervention to assess, and identification of desired outcomes from intervention implementation (Moran et al., 2020). A PICOT question may also include a time (T) component, however not all projects utilize a specific time period (Moran et al., 2020). The creation of a PICOT question supports the structural development of an evidence-based guideline.

The following PICOT question acts to guide the literature review, project development, and management: “In patients presenting emergently with airway difficulties related to angioedema (AE) (P), how would the development and implementation of evidence-based practice (EBP) guidelines for AE airway management (I) vs traditional practice (C) affect patient morbidity and mortality and airway placement metrics (O)?” Morbidity and mortality metrics are further defined as patient mortality, hypoxic brain injury, and cardiac arrest. Airway placement metrics include the time and attempts needed for definitive airway securement and the number of surgical airways. Due to the low frequency and incidence of AE, the timeline for the project will be dependent on the frequency of occurrence at the facility.

Literature Review and Synthesis

Literature Search Methods

A literature search of online databases allowed insight into airway management techniques as well as historical attempts at initiating AE guidelines. The online general academic database of EBSCOhost served as the primary source of journal articles. EBSCOhost's general academic database consists of the following databases: EBSCOhost Academic Search Complete, Newspaper Source, TOPICsearch, MasterFILE Premier (EBSCOhost, 2022). Search terms used include "angioedema," "airway management," "algorithm," "emergency management," "anesthesia," "difficult airway team," "intubation or endotracheal intubation or intratracheal," and "protocols/guidelines/procedures/policies" in various combinations. The terms "angioedema" and "airway management" resulted in 449 hits, too great a number for realistic utilization in the project. Adding the Boolean operator "AND" between the two previous terms reduced results to 20 articles. To focus on relevant articles, the complete literature search also utilized the alternate search terms and Boolean operators discussed below.

The search terms "angioedema" and "algorithm" resulted in 62 hits. Adding the Boolean operator "AND" between the previous returns narrowed the search to five articles, 3 are related to AE and medication management and two are not airway related and thus excluded from the literature review. With both terms in the title, "angioedema" and "emergency management" resulted in 11 hits. "Angioedema" AND "protocols/guidelines/procedures/policies" AND airway provided 32 results. "Difficult airway team" AND "airway management" resulted in 6 articles. "Angioedema" AND "intubation or endotracheal intubation or intratracheal" resulted in 4 articles. Secondary database searches performed on Cochrane and CINHAL via Otterbein

University's Courtright Library webpage provided similar results, with no new relevant articles obtained.

As many of the search terms resulted in large amounts of articles, the literature review used the following exclusion criteria: articles must be written in the English language with the full article available for free in a web-based platform, articles must come from a peer reviewed journal, and articles must be published post 2016, with some exceptions granted for articles that provide relevant data for the project. Other result exclusions included duplicate articles, those not specifically related to AE with airway compromise, or articles that only discussed concerns related to pediatrics. Selecting articles based on the relevance to specific anesthesia considerations further aided article narrowing. The literature review also includes works obtained via bibliographies of articles identified using the search terms specified above. A direct search by article title for these works provided access to primary source articles.

The literature review analyzes a total of twenty-eight articles, of which five are level I, or a systematic review or meta-analysis of randomized control trials (RCT), four are Level II/single RCT studies, two are level III/non-randomized control studies, seven are Level IV/case control studies, and ten are from lower level of evidence works (Appendix C & D). To fully understand the components contained in an AE best practice guideline, the literature review looks at medication management, as this differs between types of AE, methods of intubation, the creation of an emergency airway or AE cart, and lastly the creation and implementation of an AE algorithm or guideline at both the facility level and professional consortium recommendations.

Literature Review

Medication Management: Bradykinin versus Mast Cell Mediated.

Despite the high prevalence of AE, providers may misidentify or mistreat AE, resulting in delayed care and potentially devastating patient outcomes (Bernstein et al., 2017). Additionally, providers may misidentify AE as anaphylaxis due to the similarity of symptoms. However, treatment regiments between AE and anaphylaxis differ (Misra et al., 2016). Successful medication management of AE primarily depends on rapid identification of AE type (Misra et al., 2016). Angiotensin converting enzyme inhibitors (ACEi) and hereditary AE (HAE) are two of the main triggers of bradykinin (BK) mediated AE, whereas mast cell (MC) mediated AE is a histamine response often triggered by anaphylaxis or an allergic reaction (Misra et al., 2016).

Both types of AE present similarly, creating difficultly in determining the triggering cause (Misra et al., 2016). Bernstein et al. (2017) offer distinguishing features to help separate AE triggers; MC mediated AE usually presents from known allergen triggers, with urticaria and a more rapid onset, whereas BK AE usually has a slower onset (although may also have a rapid onset) with no noted pruritus (Table 1). BK AE is also more likely to present with trunk and peripheral edema compared to MC triggered AE (Bernstein et al., 2017). As quickly diagnosing the type of AE by symptoms can be challenging, suspected AE patients should initially receive anaphylaxis treatment, with histamine 1 and 2 antagonists, epinephrine as needed, and corticosteroids (Caballero et al., 2011; Misra et al., 2016; Otani et al., 2017). However, practitioners should keep in mind that MC triggered AE responds to antihistamines where BK mediated AE does not. (Caballero et al., 2011; Misra et al., 2016).

Table 1

Differentiating Between Mast Cell or Bradykinin Mediated Angioedema

Mast Cell Mediated	Bradykinin Mediated	Both
Urticaria	Abdominal Edema	Oral Edema
Itching	Peripheral Edema	Laryngeal Edema
Rapid Onset	Genitourinary Edema	Facial Edema (more likely BK)
Relieved by Epinephrine		Nausea/Vomiting (more likely MC)
Wheezing		Abdominal pain (more likely BK)
Hypotension/Shock		

Note. Table modified and adapted from Bernstein et al., 2017.

As the treatment for BK AE is more complicated, the remainder of this section focuses on medications to treat BK AE. Although not without risks, the FDA approved three drugs for the use of treatment of acute BK AE: icatibant, ecallantide, and C1 INH (Misra et al., 2016). Potential side effects for all three drugs include anaphylactoid reactions (Ecallantide only), gastrointestinal upset, headaches, and infection (Misra et al., 2016). The World Allergy Association (WAO) and the European Academy of Allergy and Clinical Immunology (EAACI) periodically release guidelines for the management of HAE (a form of BK AE). In both the 2010 and 2017 releases, WHO/EAACI do not specify which medication is best to treat acute HAE attacks, instead saying C1-INH, ecallantide, and icatibant are all acceptable choices (Bowen et al., 2010; Maurer e al., 2018). Caballero et al. (2011) also discussed the effectiveness of the above drugs. However, there is little work comparing the efficacy of the drugs against each other. As such, the following sections include a brief overview of all three medications.

Icatibant.

Yeung et al. (2018) provided a deeper look into icatibant, specifically for ACEi AE. Icatibant, a BK 2 receptor antagonist, is FDA approved for HAE, but also treats ACEi AE off label (Yeung et al., 2018). Yeung et al. (2018) discussed previous contradictory studies that utilized icatibant for ACEi AE, where one showed a significant decrease in time to resolution of AE symptoms, while the other showed no reduction versus placebo. Yeung et al. (2018) then presented three case studies with inconclusive results. In the case studies, the patients did not show any improvement in time to onset of symptom improvement (11-22 hours) or in intubation times (3-5 days post icatibant administration; Yeung et al., 2018). However, in the cases presented, the patients did not receive icatibant until well after the recommended 10-hour window of symptom onset.

Rosi-Schumacher et al. (2020) presented a meta-analysis via the PubMed and Embase databases and reported that icatibant begins to combat AE symptoms in 1-2 hours with full resolution in 1.5-8.1 hours but agreed with Yeung et al. (2018) that icatibant use in ACEi AE is inconclusive. Despite the inconclusive results, the French National Center for Angioedema recommended "B[K]2 receptor antagonists as the first-line therapy for ACEi-induced angioedema" (Brown et al., 2017, p. 1380). This recommendation may in part be due to the ease of use, and the ability for the patient to self-administer icatibant at home with a prescription (Misra et al., 2016).

C1-INH.

C1-INH regulates BK production and can reduce the intensity and duration of AE symptoms by more than 50% (Rosi-Schumacher et al., 2020). Greve et al. (2015) evaluated C1-INH treatment in patients with ACEi AE, comparing C1-INH to antihistamine and steroid

treatments. Although only a small number of patients received C1-INH compared to the control group (10 vs. 47), the study by Greve et al. (2015) showed promising results. None of the patients who received C1-INH required intubation and the time to symptom resolution was significantly faster, with the C1-INH group recovering in an average of 10 hours compared to 33 hours for the control group (Greve et al., 2015). Caballero et al. (2011) also reported positive responses to C1-INH treatment for BK AE, with a reduction in skin, gastrointestinal, and laryngeal symptoms.

In a larger, randomized, double blind study, Zuraw et al. (2010) obtained comparable results, contrasting C1-INH with a placebo for acute HAE attacks. Thirty-five participants received C1-INH for moderate to severe HAE, with time to symptom relief (not resolution) taking an average of two hours, compared to greater than four hours for the placebo group (Zuraw et al., 2010). Zuraw et al. (2010) also found a statistically significant shorter time to complete symptom resolution in the C1-INH group (12.3 v. 25 hours). The decreased time to both symptom relief and symptom resolution led Zuraw et al. (2010) to recommend C1-INH as the drug of choice for HAE treatment. In addition to C1-INH for BK inhibition, researchers are studying a new BK inhibitor which displays a reduction in AE symptoms in 15 minutes (Rosi-Schumacher et al., 2020). However, as this medication is not FDA approved, the project will not consider it for use.

Ecallantide.

Rosi-Schumacher et al. (2020) discussed the use of ecallantide, a plasma kallikrein inhibitor, to reduce AE symptoms in HAE AE and found an average time to symptom improvement of approximately 185 minutes. Bernstein et al. (2015) compared the number of patients who met ED discharge criteria (oxygen saturation >92%, blood pressure and heart rate at

age-appropriate norms) within four hours after receiving ecallantide to placebo in 50 ACEi (BK) AE patients. Of the patients who received ecallantide, ten percent more met discharge criteria within four hours versus placebo, leading Bernstein et al. (2015) to tentatively recommend ecallantide use.

However, conflicting evidence exists in ecallantide efficacy. In a double-blind randomized control trial of 79 participants, Lewis et al. (2015) compared three different doses of ecallantide (10mg, 30mg, 60mg) to placebo, using similar endpoint criteria as the Bernstein et al. (2015) study (readiness for ED discharge within six hours). Eighty eight percent of participants receiving ecallantide vs seventy two percent of the placebo group met discharge criteria within the six-hour timeframe, which was not considered statistically significant (Lewis et el., 2015). However, of those who presented with more severe AE, 100% of the ecallantide group met discharge criteria versus only 60% of the placebo group (Lewis et el., 2015).

Fresh Frozen Plasma.

Previous medication regiments for BK AE included administration of fresh frozen plasma (FFP), however, the continued use FFP is contradictory in recent studies. Rosi-Schumacher et al. (2020) and Brown et al. (2017) reported FFP administration results in symptom relief in 2-12 hours. However, the risk of potential side effects led Rosi-Schumacher et al (2020) to recommend that FFP may be administered for BK AE, as it contains C1 esterase inhibitor, but should only serve as replacement treatment when no other therapies are available. Contradictorily, FFP may worsen AE symptoms and carries the risk of viral transmission, as well as all associated blood product transfusion risk factors (Rosi-Schumacher et al., 2020).

Airway Management.

Providers have historically considered awake intubation as the gold standard for intubation in an AE or any difficult airway patient, due to the innate ability to maintain the natural airway while awake (Brambrink & Hagberg, 2013). After receiving induction medications, the upper airway structures (tongue, epiglottis, vallecula, larynx and esophagus) are prone to collapse (Cook & MacDougall-Davis, 2012). However, providers can also consider alternative intubation methods for AE intubation (Wood et al., 2013). Biro and Schlaepfer (2018) encourage the use of alternative intubation techniques, mentioning video laryngoscopy as a recommended technique for difficult airway management. To determine the current best practice method for airway securement in an AE airway, the following sections address various airway techniques.

Direct Laryngoscopy.

Although experts do not recommend direct laryngoscopy (DL) as the first "go to" for AE airways, there may be a time when DL is the only method available to the provider. A Walsh et al. (2014) study simulated Cormack - Lehane Grade 1 and Grade 3 views with a cadaver and prompted ED residents to attempt intubation via DL and DL with a gum elastic bougie (GEB). All participants attempted intubation on both views using DL or DL plus GEB methods (Walsh et al., 2014). All participants found the Grade 1 intubation to be easier than the Grade 3, with mean time to intubation approximately 30 seconds faster in the Grade 1 intubation group (Walsh et al., 2014). Additionally, the group found no difference in intubation times using a GEB compared to DL alone in a Grade 1 view, but a 41 second decrease in time to successful intubation in a Grade 3 view with GEB use (Walsh et al., 2014). As AE often presents as a Grade

3 or worse airway, the study by Walsh et al. (2014) provides a useful alternative (GEB use) to providers who only have access to DL techniques when presented with an AE airway.

Fiberoptic Bronchoscope versus Video Laryngoscopy.

Wood et al. (2013) introduced fiberoptic bronchoscope (FOB) versus video laryngoscopy (VL) techniques by discussing the historical preference of FOB utilization for AE airways to decrease manipulation to edematous airways, thus avoiding worsening irritation and swelling. Through a retrospective chart review, Wood et al. (2013) compared the FOB to VL, intubating laryngeal mask airway (LMA), and DL to determine if the FOB remained the ideal intubation method in AE management. The study found that VL took significantly less time than FOB for successful intubation, at 6.9 minutes versus 10.4 minutes, leading to the conclusion that VL is more efficient. There are multiple limitations to the Wood et al. (2013) study, one such being a small sample size of 33. Of the 33 attempts, 12 were FOB intubations and 11 were VL (the remaining 10 utilized other intubation methods; Wood et al., 2013). Additionally, the intubations were all performed by different anesthesia providers, meaning provider skill level and comfort with the appointed intubation technique could partially contribute to the time discrepancy noted between methods.

Also assessing the utilization of VL for AE airways, Driver and McGill (2017) performed a retrospective chart and ED video review of AE patients entering a level 1 trauma ED and found both DL and VL attempts had a higher success rate as a first pass attempt as versus a rescue attempt. To corroborate the benefits of GEB use from the Walsh et al. (2014), Driver and McGill (2017) used a GEB in all DL and VL attempts and had an 86% VL and 100% DL first method attempt success, while the FOB oral intubation method only had a 67% first method success rate. Additionally, time to intubation using VL was significantly shorter compared to FOB (44 v 125

seconds; Driver & McGill, 2017). Driver and McGill (2017) discussed potential limitations of the study, mainly that there was not a way to determine the location or severity of AE airway edema, which could affect the success rates of various intubation methods. However, the study was the first to comprehensively look at intubation methods in AE in a live human being (Driver & McGill, 2017).

Fiberoptic Bronchoscope versus Blind Nasal Tracheal Intubation.

Parkey et al. (2019) compared blind nasal intubation (BNI) to nasal intubation (NI) with FOB guidance, hypothesizing that FOB use may decrease the time to intubation and complications associated with NI (bleeding, turbinate damage, inadvertent esophageal intubation).To test this hypothesis, Parkey et al. (2019) evaluated ED attendings, resident physicians, and advanced medical students in the ability and time required to place a nasotracheal tube (NTT) using both BNI and FOB techniques in a mannequin with simulated AE. Prior to attempting FOB intubation, all participants received a 10 minute in service on FOB techniques and 10 minutes to practice (Parkey et al., 2019). Parkey et al. (2019) found no significant difference in time to successful intubation between the two methods, despite the participants level of medical experience. Parkey et al. (2019) made no definitive recommendations on AE NI securement methods, offering both positive and negative feedback for FOB use. FOB use provides visual feedback not available if performing a blind intubation, such as the ability to assess the airway for edema, trauma, or other pathologies, but using a FOB requires additional ongoing training for correct utilization (Parkey et al., 2019). Parkey et al. (2019) admitted the use of simulation techniques versus real AE patients as a potential limitation to the study.

Driver and McGill (2017) also compared BNI and nasal FOB intubations on human subjects and found both methods to have low first method success rates (40% and 57% respectively). Both methods of nasal intubation also took significantly longer than VL or even oral FOB techniques, with a nasal FOB taking a median of 385 seconds vs 125 seconds for an oral FOB and 315 seconds for a BNI ((Driver & McGill, 2017). Additionally, Driver and McGill (2017) found patients with longer intubation times had a higher risk of complications, such as hypoxic events and aspiration pneumonia.

Surgical Airway.

Although a more invasive airway technique, surgical airways are a potential fast and lifesaving intervention in the AE patient. With the failure of all other airway interventions, the cannot intubate, cannot ventilate (CIVA) scenario culminates in an emergency surgical airway, or cricothyroidotomy (Cric; Darby et al., 2018). Per Vuzitas et al. (2016), Cric placement takes an average of 83 seconds. However, if the patient is not at imminent risk of airway obstruction, a surgical tracheostomy is the ideal choice (Vuzitas et al., 2016).

Darby et al. (2018) evaluated emergency surgical airways (ESA) after difficult airway team (DAT) activation, with 42% related to unspecified airway edema. Per report, surgical airways more commonly occur on male, obese, and/or patients with a history of a difficult airway (Darby et al., 2018). Cricothyrotomy accounted for 91% of ESA attempts, with 85% performed by trauma surgeons. Prior to surgical airway attempts, 68% of patients had three or more intubation attempts, with 45% attempting multiple intubation methods (Darby et al., 2018). Concerningly, Darby et al. (2018) reported complications in 68% of the attempted surgical airways in the study (bleeding, multiple attempts, cardiopulmonary arrest), with only 64% of ESA successful on the first attempt and an overall 59% patient mortality rate post ESA attempt.

However, Darby et al. (2018) excluded patients with surgical airways placed in the OR and emergency airways placed in the ED or OR, as these locations are more likely to perform ESA without the assistance of a DAT. Exclusion of patients from these areas may skew the data, as ENT or trauma surgeons are more likely to perform ESA in the OR or ED and Darby et al (2018) reported these surgeons have close to 100% ESA success rates.

In ESA situations, Memorial Healthcare System utilized acute care/trauma surgery in the AE airway protocol (Lee et al., 2017). Lee et al. (2017) sought to determine the importance of the trauma team in ESA placement by completing a retrospective ESA chart review over a nine-year period. The study looked at 43 ESA, with nine of those related to AE (Lee et al., 2017). In a comparison of survival outcomes for ESA placed in the OR versus other hospital departments, ESA in the OR were 2.5 to 8 times more likely to survive to discharge (Lee et al., 2017). Lee et al. (2017) argued that ESAs should be performed by a trauma or ENT surgeon to allow for rapid placement by a skilled provider. Lee et al. (2017) did see a significantly lower mortality rate (31%) than Darby et al. (59%) (2018), but the lower rate may be due to the inclusion of ESA in a more controlled environment (the OR).

A study by Heard et al. (2009) looking at CICV situations provided additional insight into surgical airways in the AE patient. Heard et al. (2009) completed a two-phase study with anesthesia providers, utilizing both simulation mannequins and anesthetized sheep for living subjects, comparing six different surgical airway techniques. The scalpel bougie technique (midline neck incision, GEB placement through incision, railroad endotracheal tube [ETT] over GEB; Appendix E) had a 100% success rate with a mean time to placement of 39 seconds, where specific, pre-made Cric kits (Melker, Mini-trach II) took significantly longer (118 seconds and 163 seconds respectively) with 90% success rates (Heard et al., 2009). Researchers attributed the

increased time in the premade kits to operator unfamiliarity with the materials and a prolonged number of steps to use the equipment correctly and thus do not recommend the Seldinger technique as a first line Cric method (Heard et al., 2009). To simulate a difficult neck with no palpable anatomy, the study leaders injected saline into sheep necks (Heard et al., 2009). In the difficult neck, the study found only a 40% success rate with a cannula cricothyroid puncture, despite long attempt times, whereas a scalpel finger needle technique (midline neck incision with fingertip blunt dissection) had 100% success and a shorter mean time to placement (Heard et al., 2009). Heard et al. (2009) acknowledged that anesthesia providers may not feel comfortable with a scalpel. However, the study recommended the scalpel – bougie – finger technique due to minimal scalpel manipulation and anesthesia providers existing familiarity with the GEB and associated biofeedback provided by the GEB when placed in the trachea (Heard et al., 2009).

Difficult Airway Team.

Gonzalez et al. (2015) reported on the creation of a difficult airway team (DAT) at a busy Level I trauma center, which consisted of ED, anesthesia, and trauma or ENT surgeons. In the study, any provider could activate the DAT, which sent a page to the team members and an overhead hospital wide page (Gonzales et al., 2015). The activated anesthesia team member responded to the patient bedside with “a fiber optic intubation cart with video laryngoscope capability and an airway box containing additional equipment for a bedside surgical airway” (Gonzales et al., 2015, p. 195). During the one-year study period, approximately 41% (20 activations) of DAT activations occurred due to AE (Gonzales et al., 2015). FOB use accounted for 55% of intubation methods, with one patient receiving a surgical airway, and anesthesiology responsible for securing 85% of the needed airways (Gonzales et al., 2015). Gonzales et al. (2015) considered the study a successful implementation of the DAT, as there were no adverse

patient outcomes. However, the study acknowledges a similar DAT may not be feasible at all facilities, as Level I hospitals have 24-hour anesthesiology and trauma surgeons, while smaller facilities may not (Gonzales et al., 2015).

The University of Pittsburg Medical Center also created a DAT to supplement the existing rapid response team (RRT), to prompt the response of airway providers and alternative airway equipment to the patient bedside (Darby et al., 2018). The DAT consisted of 24-hour support from anesthesiology, trauma surgeons, and critical care attendings (Darby et al., 2018). The responding ICU RN brought alternative airway supplies (Glidescope, surgical airway kit, Fastrach LMA, lighted stylette, jet ventilation equipment, and various tracheostomy and ETT), with a FOB also available for use (Darby et al., 2018). Despite the creation of a DAT and immediate availability of ESA supplies, Darby et at. (2018) experienced a high mortality rate (59%), with an additional 59% experiencing cardiopulmonary arrest during DAT activation. However, chart reviews in the two year period following the initial study showed a decline in ESA and patient deaths (Darby et al., 2018). Darby et al. (2018) believed that the continued decline in ESA necessity could be related to overall institutional acceptance of DAT activation, continued airway training for providers, and increased availability and utilization of video laryngoscopy at the facility.

A study at Johns Hopkins hospital system evaluated the time to difficult airway response before and after the creation of a DAT (Pandian et al., 2019). Response times to a difficult airway call drastically decreased after implementing an in-house DAT (3.4 minutes compared to 89.2 minutes; Pandian et al., 2019). Like the studies discussed above, Johns Hopkins DAT consisted of a trauma surgeon, an anesthesia provider, critical care nurses, but also included respiratory therapists (Pandian et al, 2019). Like the Darby et al. (2018) and Gonzalez et al.

(2015) studies, Pandian et al. (2019) admitted the potential limitations of implementing a similar DAT in smaller facilities, due to lack of 24 hour availability of all services.

Implementation of an Angioedema Guideline.

Due to the infrequent occurrence of AE, clinical trials for AE guideline implementation prove to be difficult. As such, many of the guidelines retrieved in the literature are based on case study review and consensus statements from AE expert opinion. Unlike other life-threatening emergencies, such as cardiac arrest and the American Heart Association's Advanced Cardiac Life Support (ACLS), there is not a similar national algorithm for BK AE management in the United States (Brown, 2017). Bernstein et al. (2017) suggested the lack of algorithms is due to the infrequency of hospital ED visits for BK AE. Despite the lack of a nationwide AE algorithm, individual hospital systems have implemented system specific AE guidelines (Jaiganesh et al., 2012; Lee et al., 2017; Long et al., 2019; Pandian et al., 2019).

Confirming statements about the lack of AE guidelines/algorithms, Jaiganesh et al. (2012) conducted a survey of 34 United Kingdom Hospital Trusts with associated immunodeficiency departments to determine the presence of an AE protocol or guideline, specifically around the usage of C1-INH. Of the hospitals surveyed, only half had a guideline for C1-INH administration and the medication immediately available for ED use (Jaiganesh et al., 2012). Jaiganesh al. (2012) proposed an AE guideline, but at the time of article publication, the College of Emergency Medicine had not approved the guideline for use. As Jaiganesh et al. (2012) had not implemented the guideline, the article stressed the importance of the guideline itself instead of insight into the success or failure of guideline implementation.

Similar to the Jaiganesh et al. (2012) findings, Bernstein et al. (2017) looked at BK AE management in the ED and found 50% of the hospitals surveyed did not have guidelines for AE

medication or airway management. In addition, the necessary medications for BK AE were not readily available in the ED, with the medications instead stored in the main pharmacy (Bernstein et al., 2017). Bernstein et al. (2017) concluded that the "lack of protocols and access to medications can lead to treatment errors and poor outcomes for ED patients" (p. 3). To establish an AE guideline or protocol, Bernstein et al. (2017) suggested including airway management, MC mediated medications, and BK mediated medications. In concordance with previously mentioned authors, Bernstein et al. (2017) recognized that AE can rapidly lead to an unsafe airway and advocated for early invasive airway placement as needed, either via ETT, NTT or surgical airway. Bernstein et al. (2017) believed oral cavity swelling can determine the necessity of intubation, with intubation unnecessary if edema remains in front of the teeth (may be medically managed), and intubation likely if swelling is behind the teeth. Bernstein et al. (2017) suggested NTT placement, specifically awake NTT, as the preferred option, as tongue and lip swelling may obstruct passage of an ETT. Visualization or DL attempts should not occur prior to NTT placement due to potential for increased airway swelling (Bernstein et al., 2017). Additionally, Bernstein et al. (2017) advised the presence of an airway team prepared to perform a surgical airway if needed. If the patient does not require immediate airway interventions, Bernstein et al. (2017) recommended similar medication management as discussed in the previous section.

In a retroactive case-controlled study, Pandian et al. (2019) showed that the implementation of a specific AE management protocol can combat delays in care and misdiagnosis. Pandian et al. (2019) implemented a DAT at Johns Hopkins, created an emergency airway cart (EAC) and established standardized methods for AE airway management. Following the implementation of a full AE program, the study found that program creation increased

successful airway placement while also decreasing the number of attempts needed (Pandian et al., 2019). Additionally, the Johns Hopkins study also found a reduction in provider response times to the patient bedside after the implementation of an AE protocol (Pandian et al., 2019). Pandian et al. (2019) reported one reason for the reduction in response times and decrease in time to establish a definitive airway was the creation of the EAC, as the carts provided a consolidated area for airway supplies, reducing the time and effort required to gather needed airway materials.

Lee et al. (2017) discussed the AE protocol in place at Memorial Healthcare System, where suspected AE fell into three intervention categories. If only lip edema is present and intubation is needed, the ED provider had one attempt at intubation before contacting anesthesia for assistance (Lee et al., 2017). With the presence of tongue edema and a Mallampati Class I or II view, the ED provider had the option to attempt an airway or call anesthesia, but a Class III or IV view required immediate involvement of anesthesia (Lee et al., 2017). Anesthesia then determined the necessity of ESA/trauma assistance (Lee et al., 2017). Patients presenting in extremis required immediate activation of both the trauma surgeon and anesthesia (Lee et al., 2017). In addition to rapid surgical and anesthesia involvement, Memorial's protocol involved immediate patient transport to the OR for optimal high risk airway conditions (Lee et al., 2017). Through the early identification of AE/difficult airways with appropriate team activation, Memorial was able to decrease patient mortality, however implementing a similar comprehensive plan may not be possible in all facilities, secondary to provider availability (Lee et al., 2017).

Otani et al. (2017) looked at patient perspectives on ED HAE treatment after the 2009 implementation of nationwide FDA HAE guidelines. Six percent of study participants reported

improved HAE care, however 39% reported worse or unchanged ED care (Otani et al., 2017). The main patient concern after guideline implementation involved continued lack of ED provider knowledge of HAE, included incorrect treatment medications (Otani et al., 2017). Otani et al. (2017) suggested delays in care were related to "lack of [provider] awareness," "lack of [provider] awareness of guidelines for treatment," and "inability [of patients] to access effective…therapies" (p. 133). Although the Otani et al. (2017) study looked at patient perceptions, it provides insightful evidence for areas of improvement when implementing an AE guideline.

International Angioedema Consensus Statements.

As mentioned above, although there is not a "gold standard" for AE management like ACLS, different medical organizations offer consensus statements for appropriate AE management. Fisher and Abukhdeir (2016) offered guideline suggestions, with airway securement being the number one priority. Like Bernstein et al. (2017), Fisher and Abukhdeir (2016) recommended awake NTT, as standard intubation techniques can worsen airway obstruction and result in a more difficult intubation. Attempted use of laryngeal mask airways (LMA) also resulted in decreased airway success, due to laryngeal swelling (Fisher & Abukhdeir, 2016). As in previously discussed articles, anesthesia ideally performs the intubation with a surgeon immediately available (Fisher & Abukhdeir, 2016). Medication treatments agree with that described above. Fisher and Abukhdeir (2016) provided two detailed diagram algorithms related to AE care; one that discussed appropriate interventions based on the severity of airway involvement and one covering medication management and patient disposition (ICU, medical, or observation units) post ED stabilization. Italian (Cicardi et al., 2013), British

(Jaiganesh et al., 2013), and American (Long et al., 2019) expert committees all offered similar algorithm guidelines for AE care.

Moellman et al. (2014) published a consensus statement on AE management created by emergency medicine, allergy, and immunology physicians. Initial treatment should focus on airway assessment, using a FOB to determine the severity of laryngeal swelling (Moellman et al., 2014). Airway assessment via FOB without placement of a definitive airway directly contradicts previous articles discussed, which stressed the importance of minimal airway manipulation prior to ETT/NTT placement to avoid worsening airway edema. However, Moellman et al. (2014) agreed with early intubation, avoidance of LMA use, and initial treatment with anaphylaxis medications. Moellman et al. (2014) suggested the acceptability of administering succinylcholine with caution and etomidate or lower dose ketamine (<1mg/kg) for intubation to preserve airway reflexes. However, an awake FOB or VL intubation may be a better option, premedicating with atomized nasal vasoconstrictors and intravenous glycopyrrolate (Moellman et al., 2014). Moellman et al. (2014) recommended a premade Cric kit for potential surgical airways, but do not delineate provider responsibility for performing the surgical airway. Deviating from other guidelines, Moellman et al. (2014) named FFP as the most practical BK AE treatment, arguing that there is not enough evidence to recommend the use of C1-INH, icatibant, or ecallantide. However, the difference in medication recommendations may be due to the earlier publication date of the Moellman article, and thus potential increased data availability of drug efficacies in the articles discussed in earlier sections.

A 2021 American Academy of Emergency Medicine (AAEM) Clinical Practice Committee consensus statement provided up to date recommendations on ACEi AE (a form of BK AE) management (Rosenbaum et al., 2021). Airway assessment remained the number one

priority, with the following symptoms indicating laryngeal or posterior pharyngeal involvement, potentially indicating the need for intubation: dysphagia, dysphonia, drooling, hoarseness, stridor, or the perception of an object retained in the throat (Rosenbaum et al., 2021). Like Moellman et al. (2014), Rosenbaum et al. (2021) recommended FOB use via the nose to assess airway involvement but stipulated the necessity for a skilled provider and immediate availability of both intubation and surgical airway equipment. The 2021 consensus statement did change medication management slightly, especially the previously recommended initial treatment with anaphylaxis medications (Rosenbaum et al., 2021). The risk to benefit ratio remains high, corticosteroids and antihistamines remain recommended, however, the risks of epinephrine administration outweigh benefits except in cases of extreme airway involvement (Rosenbaum et al., 2021). As such, the 2021 AAEM guidelines recommended epinephrine use only in severe AE cases (Rosenbaum et al., 2021). The AAEM also does not recommend a specific medication for treatment of ACEi-AE due to the prohibitive cost of the medications and conflicting results in medication efficacy studies on C1-INH, icatibant, ecallantide, and FFP (Rosenbaum et al., 2021).

Long et al. (2019) presented a consensus statement from case reports and randomized control trials obtained from PubMed and Google Scholar that support the works of Bernstein et al. (2021) and Moellman et al. (2014) presented above, with the airway being the primary focus of an AE patient. Long et al. (2019) gave additional suggestions for determining the need for airway interventions, by asking the patient to phonate the letter “E,” as the patient with laryngeal edema cannot produce this sound. Agreeing with Rosenbaum et al. (2021), facial swelling should trigger an airway assessment with the FOB, despite mentioning the potential for worsening edema with airway manipulation (Long et al., 2019). Long et al. (2019) also discussed the

inconsistent reporting of results for medication treatment of AE, encouraging provider focus on airway management rather than medication treatment, as the efficacy of medications is uncertain.

Literature Summary

Although discussed in many of the works, there appeared to be no consensus for an ideal intubation method for AE. Seven articles continued to recommend FOB as the gold standard, however only two of these articles are actual research studies, the remainder only recommend or utilized the FOB in the guideline recommendations because the FOB is the "gold standard" for AE/difficult airway situations. Two articles believed VL is the optimal method based on the conducted study, and the remainder do not specify. One noted trend, however, is that older works leaned towards FOB usage while more recent recommendations seem to push for VL use in AE airway management. There also appeared to be a lack of agreement as to whether an ETT or NTT allows for the best chance of airway success, as this may be more patient specific, but more of the articles discussed the placement of NTT over ETT.

Despite the lack of consensus in airway securement methods, all the included articles agreed in the necessity for early, aggressive airway management, including surgical airways. The general consensus of the retrieved articles suggested surgical airway responsibility lies with either ENT or the trauma/acute care surgeon and should be placed in an OR setting but admitted that all facilities may not have immediate access to ENT or trauma surgeons. When 24-hour ENT or trauma is not available, the articles deferred surgical airway intervention to anesthesiology, and thus stress the importance for anesthesia providers to also be skilled in invasive airway techniques.

Likewise, there appeared to be no clear-cut answer for medication choice. To date, there are no studies which compare the three BK AE medications (C1 INH, ecallantide, icatibant)

against each other, with studies instead comparing the individual drugs to placebo (Bernstein et al., 2017). Additionally, none of the articles discovered in the literature review recommended the use of one medication over the others, instead recommending medication selection to be based on both medication availability and individual patient characteristics (i.e., not all medications are appropriate for pregnant or pediatric patients).

However, Bernstein et al. (2017) provided a comparative chart on time to symptom relief after receiving medication, with plasma derived C1-INH being the shortest at 30-48 minutes and icatibant requiring a median time of 2 hours to symptom relief. Ecallantide carries the risk of anaphylactoid reactions and C1-INH has potential allergic reactions depending on form (plasma derived has standard blood product considerations and recombinant reacts in people with rabbit allergies; Misra et al., 2016).

Despite discrepancies in recommended medication treatments and airway securement techniques, literature suggestions agreed on the need for clearly defined AE management guidelines to reduce time to intervention, cost of treatment, and potential harm to patients. Creation of a full AE guideline allowed for increased team building and comfort in knowing individual job roles. The guideline acts to delineate expectations for each department as well as identify appropriate medications and airway interventions based on updated evidence-based practice.

Analyze

Collect Baseline Data

After obtaining the appropriate Institutional Review Board (IRB) approvals, the project team will complete a retrospective chart review of ED visits and hospitalized patients to determine the number of AE cases within the last five years. To obtain the appropriate

information, the project team will search for charts with ICD 10 code T78.3 angioneurotic edema, including the subcodes T78.3XXA, T78.3XXD and T78.3XXS (ICDcodes.com, n.d.; ICD10Data, n.d.). Once identified, the project team will then evaluate the AE charts to determine the number of cases requiring airway intervention, number of attempts made for airway securement, and cases requiring surgical or emergency/rescue airways. Finally, the chart review will look at the time from patient arrival to the time of definitive airway placement along with mortality and morbidity (hypoxic brain injury and cardiac arrest) associated with airway securement.

Determine Influential Factors

As previously mentioned, through informal departmental meetings with anesthesia department representatives, anesthesia providers believe ED providers to have less emergent airway experience, due to the presence of newer providers/residents, and that ED providers do not call for airway assistance until after the patient is experiencing symptoms of respiratory distress. Data obtained through the literature supports anesthesia provider concerns about experience level (Brambrink & Hagberg, 2013). In Benumof and Hagberg's *Airway Management* textbook for anesthesia providers, Brambrink and Hagberg (2013) discuss different variables that can contribute to failed or difficult intubations, such as differing skill levels in intubation practice. As the first attempt on an airway is the best attempt at success, laryngoscopy attempts should be kept to a minimum, with the most experienced provider making the first attempt (Brambrink & Hagberg, 2013). Laryngoscopy attempts by unskilled providers increases the risk of laryngeal edema and bleeding, which can lead to complete airway obstruction (Brambrink & Hagberg, 2013). To reduce the effects of varying ED provider experience, anesthesia providers believe that the anesthesia team should be responsible for AE airway interventions.

Develop

Select Solution (Guideline Development)

To best serve all team members and patients, the needs analysis supports the development of a multidisciplinary EBP guideline for AE management. After completing the literature review, looking for current EBP on the various aspects of AE management, the project team created a guideline for implementation. Appendix F and G contain a graphic algorithm and step by step instructions for staff distribution. The following sections will address each aspect of implementation, along with responsible parties and rationale behind each choice.

Emergency Department Providers

Interventions.

As ED providers are often the first point of contact, identification of an AE patient relies on ED diagnosis and early recognition. ED staff will obtain vital signs with pulse oximetry and end tidal carbon dioxide (ETCO2) readings, as ETCO2 readings are a more reliable indicator of ventilatory status (Moellman et al., 2014). ED providers will also obtain as thorough an exam and health history as possible, including the presence of lip/facial swelling, ability to phonate the letter E, gastrointestinal symptoms, speed of onset, itching, personal or familial history of AE, current medications, recent trauma, and any home remedies attempted prior to ED presentation (Long et al., 2019).

Consumption of ACEi or ARBs may indicate a positive AE case. Recent trauma is a known trigger for HAE (Long et al., 2019). Speed of onset is important to note, as HAE usually has a faster onset than BK AE (Long et al., 2019). Phonation is an important diagnostic indicator for airway involvement in AE, as the ability to phonate the letter E with a higher pitch is a strong indicator that there is no laryngeal edema (Long et al., 2019). However, the presence of stridor,

hoarseness, or vocal quality changes may indicate the need for airway interventions (Long et al., 2019).

If the ED provider identifies the possibility of airway involvement, providers should contact anesthesia immediately via an overhead and direct page to the difficult airway team. The ED provider should not attempt to manipulate the airway, allowing for anesthesia to have the first look/first attempt for the best chance of success (Bernstein et al., 2017; Cook & MacDougall-Douglass, 20212; Darby, et al., 2018; Lee et al., 2017; Rosi-Schumacher et al., 2020). The ED is also responsible for bringing the AEC to the patient's bedside. While waiting for an anesthesia provider, the ED may deliver supplemental oxygen via face mask or nasal cannula if needed. Nasal trumpets and positive pressure ventilation do not aid in oxygen delivery for AE patients and may cause more harm than good (Moellman et al., 2014). The ED may also begin medication administration (see medication section).

If the patient rapidly decompensates, the ED provider may place an infraglottic, transtracheal intravenous (IV) catheter and begin jet ventilation. The project team selected the utilization of IV catheters for emergency cricothyrotomy due to ease of use and easily obtainable supplies (14g IV catheters). Use of a temporary infraglottic airway is to conserve first pass airway attempt for anesthesia, as subsequent manipulations of the airway may create increased intubation difficulties. Higher tracheal pressures created via jet ventilation may also serve to open the glottis and make for easier glottic landmark identification (Heard et al., 2009). If ED providers recognize airway compromise quickly, there is adequate time for anesthesia to respond to an AE case. However, as jet ventilation is safe for partial airway obstruction but is contraindicated in complete obstructions, the ED provider may attempt airway placement in extreme situations only (Heard et al., 2009).

Medications.

All medications for AE will be available in the angioedema cart (AEC). Providers should treat all patients who present with severe airway involvement as anaphylaxis first, with administration of intravenous steroids, antihistamines, and intravenous fluids and judicious administration of epinephrine based on severity of symptoms (Long et al., 2019; Rosenbaum et al., 2021). The need for immediate airway interventions supersedes attempts to determine anaphylaxis versus AE. However, if the swelling is due to BKAE/ACEi AE, the symptoms will not respond to the use of epinephrine (Rosenbaum et al, 2021).

If the patient is not in immediate airway distress, then the provider may begin treating AE. Research has shown that if airway swelling is present only in the lips, then the patient will likely only need medications and not intubation (Bernstein et al. 2017; Long et al., 209). As discussed in the literature review, there is no clear-cut medication choice between icatibant, C1-INH, or ecallantide in patient outcomes. This project will utilize icatibant as the drug of choice, as the medication has no known allergic reactions and is available on the hospital formulary (Maurer, 2018; Misra et al., 2016; OhioHealth, 2022).

ED providers may administer an IV antisialagogue. The guideline recommends the use of glycopyrrolate due to lower potential side effects (Gil & Diemuncsch, 2013). In anticipation of the need for nasal intubation, ED staff should also administer an oxymetazoline spray to the nostrils bilaterally.

Anesthesia Providers

Airway Techniques.

As AE presents as a challenging airway, anesthesia providers should attempt (within reason accounting for patient safety) to transport the patient to the trauma OR prior to airway

manipulation for greater access to resources and ability to rapidly convert to a surgical airway if necessary (Cook & MacDougall-Douglas, 2012; Lee et al., 2017). If the medical team deems the patient too unstable to transport or if the trauma OR is unavailable, airway interventions will take place at the patient's bedside, as all supplies are available in the AEC, with multiple providers present to assist.

Historically, the gold standard for AE or difficult airway intubations was an awake nasal intubation via FOB as BK AE is less likely to have nasopharyngeal involvement versus oral swelling (Vuzutas & Sarafoleanu, 2016; Bernstein et al., 2017). However, multiple newer studies show that video laryngoscopy provides the same first pass success rates with less time needed to obtain a definitive airway (Darby et al., 2018; Driver & McGill, 2017; Wood et al., 2013). As such, the project guideline proposes the use of a video laryngoscope for AE airway attempts. The decision to place an NTT or ETT will defer to individual patient presentation, however the provider should prepare for the potential of placing an NTT utilizing a VL for visualization. Regardless of the method of intubation selected, the patient should be prepared for an awake intubation, to allow the patient to retain protective airway reflexes in the event of placement failure (Gil & Diemuncsch, 2013; Long et al., 2019; Moellman et al., 2014).

If the anesthesia provider is unable to secure an airway and needs to resort to a surgical airway, the anesthetist should utilize the scalpel bougie technique taught during skills sessions. The anesthesia provider should mark the cricothyroid membrane on the patient prior to attempting any airway interventions, to allow for rapid identification in the event of a failed intubation and patient decompensation (Moellman et al., 2014). The project promotes the use of scalpel bougie technique due to decreased scalpel manipulation skills required and shorter time to establishing an airway versus a premade Cric kit (Heard et al., 2009).

Induction Medications.

Although guideline recommendations call for the use of video laryngoscopy for airway placement, anesthesia providers should prepare for all potential scenarios and prepare the patient for potential nasal intubation and a surgical airway. Historical use shows the following medications may aid the anesthesia provider in providing patient relaxation for definitive airway placement: midazolam, fentanyl, ketamine and dexmedetomidine (Gil & Diemuncsch, 2013). These medications offer patient amnesia, algesia, and hypnosis, as well as antitussive effects, while preserving the patients innate ability to maintain the airway (Gil & Diemuncsch, 2013; Long et al., 2019; Moellman et al., 2014). However, as ketamine may increase oral secretions, recommendations suggest concurrent administration of an antisialagogue such as glycopyrrolate (Gil & Diemuncsch, 2013).

Implementation Plan

Sample/Setting

The target facility for the proposed project is a hospital system located in a large city in the Midwest, with multiple facilities ranging from small to midsized and rural to intercity. Initial guideline implementation will occur in a mid-sized, inner city, level one trauma hospital. Sample size will be dependent on the number of patients that present to the ED with AE during the trial period. The target audience for guideline implementation is all staff who may provide direct, first line care for a patient with AE: ED providers, ED nursing staff, anesthesiologists, certified registered nurse anesthetists (CRNA), student registered nurse anesthetists (SRNA), respiratory therapists (RT), Intensive Care Unit (ICU) providers and nurses, and pharmacy staff.

Develop Implementation Plan

Guideline implementation will consist of two phases, staff training and actual guideline implementation with outcome tracking. Initial training will consist of an email to all targeted staff, explaining the guideline itself and the expected training offered for each department. Guideline implementation will occur after two months of staff training opportunities, with a goal of a minimum of 75% of respective staff receiving skills and guideline training. Please refer to the Execute section for training and specifics of guideline implementation.

Budget and Barriers to Implementation

Budget.

Financial.

The implementation of an AE management guideline does present disadvantages to the hospital, such as cost for training and creation of the airway cart. The cost of simulation equipment alone is potentially over $7,000 (GTSimulators, 2022; Table 2). However, the project avoids the cost for simulation equipment purchase, as the project hospital owns similar training mannequins.

Table 2

Simulation Materials

“Broncho Boy”	$3,782
Difficult Airway Simulator	$2,400
“Cric Simulator”	$ 837

(GTSimulators, 2022)

Creation of the AEC also comes at an expense. The AE cart serves to create a more organized and easily accessible location for the medications as well as intubation instruments.

Purchase of the cart itself is $1,250 with an additional approximate cost of $9000 for cart supplies (Appendix H; Global, 2022). The facility would need to purchase the cart itself and the King Vision LED VL. The project selected the King Vision LED VL for use due to its portability and because the King Vision LED VL utilizes disposable battery power, which eliminates charging concerns. The $9000 supply price is not a true reflection of cost to the facility, as the medications are the most expensive cart inclusion, and the facility already carries these medications on formulary, making the true facility cost approximately $2,800. Additional costs related to the AEC include the maintenance of equipment and monitoring of drug expiration dates.

Cost considerations also include staff salaries for training, consisting of the hourly rate for ENT/trauma surgeons to provide training for surgical airway interventions, anesthesia providers to practice skills, and the simulation lab staff required to run the equipment. Anticipated training time for airway interventions is approximately two hours. The average hourly wage for CRNAs in Ohio is approximately $105 per hour (CRNA, 2022). The project hospital has 42 CRNAs on staff. Cost for all CRNAs to complete the training is $8,820 if all providers attend the training while off shift. The average anesthesiologist salary in Ohio is approximately $160 per hour (Anesthesiologist, 2022). The hospital has 20 anesthesiologists on staff. If all attend the same training as the CNRAs, the cost would be an additional $6,400.

To facilitate learning, the project team will divide the anesthesia providers into groups of eight participants, meaning there will be a total of six training sessions. Each session requires the presence of one ENT or trauma surgeon to instruct and one simulation lab RN. The average hourly rate for an ENT surgeon is $154 per hour and a trauma surgeon is $109 per hour for a surgeon average of $ 132 per hour (Otolaryngologist, 2022; Trauma, 2022). The cost for one

surgeon present at all six training sessions is $1,584. The cost for the simulation lab RN, with an Ohio average salary of $36 per hour, totals $432 for all six training sessions (BSN, 2022). Total staff training costs are $17,236.

ED providers will attend a short in-service to refresh skills on providing transtracheal, infraglottic JET ventilation. The average hourly wage of an ED physician in Ohio is $160 per hour (Emergency, 2022). As the in-service will be less than 30 minutes, the ED staff may attend this training while on a regularly scheduled shift, thus not incurring additional project costs. Additionally, affected ED clinical providers (ED, ED RN, and RT) will receive a short email describing each provider's role and expectations in the guideline. As staff check emails on a regularly scheduled shift, there will be no added cost for guideline delineation.

The proposed guideline instructs ED providers not to attempt an AE airway intervention unless there is immediate threat to loss of life, instead consulting anesthesia for airway placement, meaning a dedicated anesthesia provider needs to be available at all times. As such, the appointed anesthesia provider cannot cover routine surgical cases (Pandian et al., 2019). At a CNRA salary, the cost per 12-hour shift to remain out of ratio is $1,260. However, this staff member may be available to assist other anesthesia providers or act as charge CNRA. As the charge CRNA is out of ratio per normal hospital operations, there would be no added cost for this portion of guideline implementation.

Although implementation appears costly at first glance, providing clear, delineated guidance for AE care leads to a reduction in invasive airways needed (and thus decreased ICU stays), decreased patient morbidity and mortality, and decreased hospital expenses. Pandian et al. (2019) showed that the creation of an AEC leads to a reduction in response times and decrease in time to establish a definitive airway. Research also shows that early identification of AE along

with a targeted approach to management can shorten time and severity of AE attacks (Javaud et al., 2015). Evaluating the cost of negative AE outcomes also aids in justifying the cost of guideline implementation. The average cost of an ICU stay for AE with mechanical ventilation is $42,570 (with an average 14 day stay) per patient (Dasta et al., 2005). Early implementation of AE interventions may serve to reduce or eliminate the need for long term ventilation and increased patient morbidity stemming from the lack of best practice treatments (Dasta et al., 2005).

The other potential inflated cost of inadequate AE management is the risk of litigation. The American Society of Anesthesiologists' Closed Claims Project (ASACCP) tracks litigation against anesthesia providers. The ASACCP demonstrates that inadequate ventilation and substandard care are two main indicators for litigation (Cook & MacDougall-Davis, 2012). In 2018, there was a total of over four billion dollars paid out in medical malpractice claims, with the average amount per occurrence being just under $350,000 (Cappellino, 2021). However, when looking at claims paid for anesthesia involved events, the average payout for significant permanent injury is around $950,000 for a CRNA led case and is over one million dollars per occurrence when an anesthesia resident participates in patient care (Jordan et al., 2013; Kang et al., 2020).

Non-Financial.

Consideration of financial costs is important, but there are also important non-financial implications to consider in implementing a new AE guideline, with the largest non-financial impact on staff resources. The creation and upkeep of the AEC adds additional job responsibilities to the nursing, pharmacy, and respiratory teams, as each is responsible for monitoring medication outdates, stocking the cart, and checking the airway equipment.

Departmental leadership will also be responsible for ensuring task completion in a timely manner. Additionally, any time for staff training or completion of AEC monitoring tasks takes providers away from patients.

Ethical Considerations.

Prior to project implementation, IRB review will include an ethics review. The project team will complete all chart reviews, both retro and prospective, using VMWare Horizon Client encryption while accessing Epic CareConnect. All recorded and utilized data will be patient deidentified prior to publication or outcome dissemination. The project does not require patient consent for participation as all patients with AE will receive the same EBP treatment modalities. If there is a drastic increase in adverse events during the project period, the project team and facility will stop and revaluate interventions to determine if continuation is possible with modifications.

Execute

Gain Commitment

Creating an AE guideline requires the buy in of primary and secondary stakeholders. Rai et al. (2004) propose successful management of AE patients must include a multidisciplinary approach, including ED, surgical, anesthesia, and ICU team members. ED and anesthesia providers are the initial primary stakeholders, as the ED is the first point of patient contact and anesthesia providers are responsible for securing difficult airways. The guideline also needs complete buy in from administration and departmental leaders. Administrator approval is necessary to receive guideline funding and department leadership assistance will be necessary to disseminate guideline information and enforcement when enacted.

Ancillary teams must also be involved in the process, as the guideline includes the creation of an AE cart for the ED. The AE cart contains medications and equipment, necessitating the involvement of pharmacy to regulate medications, central supply to order the cart and supplies, and nursing or respiratory therapy to complete outdate checks on the cart. Effectual implementation of a new guideline requires all members to work together towards the goal of patient safety.

Emergency Department

ED providers should have excellent airway management skills with specialist back up, as the first point of contact for a patient experiencing an AE emergency is the ED (Rajan et al., 2020). Following this recommendation, the guideline advises ED personnel call the anesthesia team for AE airway assistance, utilizing the expertise of anesthesia providers. A prompt response to the AE airway necessitates a working collaboration between ED and anesthesia departments.

ED nurses also have a role in the proposed AE guideline. The guideline creates the AEC with all supplies needed for medicating and securing an airway in AE. Since the AEC contains medications, the ED nurse will be responsible for monthly expired medication checks, looking at a sticker placed by pharmacy on the outside of the cart identifying the earliest medication expiry date in the cart. When the sticker shows an expiring medication, the ED nurse notifies the pharmacy of the need for new medications. The ED nurse will also check non medication materials in the AEC on a quarterly basis for expired items. To aid in AEC check completion communication between charge nurses, there will be a monthly sign off form on the top of the cart, with the expectation for the charge RN on the last day of the month to confirm the AEC sticker remains in date.

Anesthesia Department

Multiple areas in the anesthesia department have a stake in the proposed guideline. The guideline tasks both anesthesiologists and CRNAs in placing AE airways. AE can quickly lead to airway compromise, necessitating all providers responsible for airway interventions, including all members of the anesthesia team, to understand the implications and interventions related to an AE airway (Misra et al., 2016). To ensure competence in AE airway interventions, anesthesia providers will undergo additional sim lab training in AE airway intubation using VL and emergency surgical airway techniques. Additionally, the guideline also affects anesthesia technicians (AT), as ATs will assist in restocking the AEC.

ENT or Trauma Team

Previous research at large educational facilities involving AE airway guideline development suggest the utilization of otolaryngologists (ENT) or trauma surgeons to intervene in AE airway emergencies (Darby et al., 2018; Lee et al., 2017; Pandian et al., 2019; Rosi-Schumacher et al., 2021). The goal of the proposed guideline involves eventual implementation in smaller hospitals in the system without 24-hour availability of ENT or trauma surgeons. As such, the anesthesia team must be confident in the ability to provide all manner of difficult or surgical airway interventions. To ensure anesthesia provider confidence, ENT or trauma surgeons will provide in depth training for surgical airway techniques.

Administration/Leadership

Administrator approval is necessary to receive guideline funding. Department leadership assistance from each of the above identified departments will be necessary to disseminate guideline information and enforcement when enacted. Department leaders will be responsible for

ensuring AE guideline distribution in unit employee emails and will serve as a mediator to gather any staff questions and concerns to report back to the project team.

Pharmacy

The AEC contains medications to treat AE, necessitating the involvement of the pharmacy department. Pharmacy orders all needed medications and can notify the guideline creator if desired/best practice medications are unavailable as nonformulary or from supply line issues. Pharmacy will be responsible for ordering all required medications and stocking the medication drawer in the AEC. To assist the ED nurses with outdate medication checks, the pharmacy locks the medication drawer when complete, placing a sticker on the outside of the AEC with the next expiring medication, similar to code cart setups. When the ED nurse notifies the pharmacy of an expiring medication drawer, pharmacy replaces the drawer with usable medications.

Respiratory Therapy

Respiratory therapy (RT) buy in is a key factor in any airway management guideline. As RT is the most familiar with airway equipment, the RT will be responsible for daily checks to ensure the working order of the video laryngoscope. In the event of an AE case, RT will be immediately available at the patient bedside to set up intubation equipment for anesthesia provider use and to assist the responding anesthesia provider as needed. After an airway intervention, the RT is responsible for appropriately restocking the cart with any used airway equipment.

Education

As mentioned previously, anesthesia providers need to obtain and maintain competency on a variety of airway intervention skills (Pandian et al., 2019). Anesthesia providers should

attend continuing didactic and hands on sessions, using high fidelity simulation mannequins (Pandian et al., 2019). In addition, ED providers will receive additional education on AE medication and placing a needle cricothyrotomy with JET ventilation as a last resort prior to anesthesia arrival. Use of training facilities and simulation necessitates the involvement of the hospital education department.

Intensive Care Unit

The implementation of an AE airway guideline requires buy in from the Intensive Care Unit (ICU), as patients requiring airway interventions usually require ICU admission until airway swelling decreases. ICU physicians and nurses help to manage and monitor the patient's airway until a noted decrease in laryngeal edema and presence of an endotracheal cuff leak, marking safer conditions for patient extubation. If the presenting AE is the patients first episode, the ICU team plays an important part in discovering the reason for AE and methods to decrease risk of recurrence.

Ancillary Departments

Central supply plays a vital role in the creation of the AEC. Both the cart itself and the materials stocked inside the AEC come from central supply. The central supply ordering team will ensure all materials are available to complete the creation of the cart. In the event of AEC usage, central supply restocks all utilized items other than intubation supplies and returns the cart to the appropriate location in the ED. Support from the information technology (IT) department will be crucial for both the retrospective and prospective chart reviews to track AE cases.

Approval Process

Approval of an AE management guideline is a multifactorial process. Initial steps involve discussions with all identified stakeholders to ensure all agree with expected roles and

responsibilities. Implementation of the AE guideline places additional time needs on the various departments. Additional discussions and changes to the guideline may be required before all parties are content with the assigned roles.

After all stakeholders agree to the guideline's acceptability, the project team will present the guideline to the hospital review board. At that time, additional, non-affected departments and administration can present concerns or suggestions regarding implementation. Involved parties can then complete any necessary additional changes at that time before the guideline "go live" date. The hospital ethics committee will also review the guideline prior to implementation to ensure patient safety. Additional reviews of the guideline will occur at the one month, six month, and one year time mark to ensure the guideline produces the desired result of decreased morbidity and mortality related to AE. If morbidity or mortality increase or does not decrease from current levels, then the guideline may be reevaluated for potential needed modifications.

Execute Plan

Staff Training

ED staff will attend a skills refresher in-service training on JET ventilation. As this training will be short, the ED staff may complete this training while on a regularly scheduled shift. ED staff will also review the AE guideline, with particular attention placed on the ED provider role in an AE airway emergency. Training for needle cricothyrotomy and jet ventilation will occur using the "Cric Simulator."

Anesthesia providers will attend a two-hour training session led by the project team and either an ENT or trauma surgeon. ED providers may choose to attend this training as well. The training session will start with a discussion on the guideline, explaining reasonings and the anesthesia provider's role. The surgeon will conduct the remainder of the session, with a

demonstration of the finger – scalpel – bougie emergency surgical airway technique followed by time for each provider to practice the technique on the "Cric Simulator" with surgeon critique. Participants will also receive the opportunity to practice VL intubation skills using the difficult airway simulator set to mimic a severe AE airway, as well as the "Broncho Boy" mannequin for nasal intubation practice.

Anesthesia training will occur in the hospital simulation classroom, with assistance from the education staff to ensure proper usage of all equipment. Along with all required mannequins, the simulation space has a video laryngoscope available for training purposes. ED/ICU RN, RT, and pharmacy training will consist of an email only, with the guideline and job roles explained.

Guideline Implementation

After a two-month training period, 75% of affected staff will complete guideline training and skill remediation training. At that time, the guideline will "go live" and providers should treat any suspected AE case according to the guideline. The project team will post copies of the guideline at all ED work stations, as well as ED, RT, and anesthesia break rooms and appropriate locker rooms. The guideline will also be available on top of the AEC for rapid use. Providers should consider any cases of airway swelling as suspicious for AE, prompting use of the AE guideline. The project team and representatives from pharmacy and central supply will create the AEC during the staff training period, ensuring that all supplies and medications are available for use on the go live date.

Monitoring Impact

Data Collection

To monitor patient outcomes post AE guideline implementation, the project team will complete chart reviews for AE cases, again using ICD 10 code T78.3 angioneurotic edema,

including the subcodes T78.3XXA, T78.3XXD and T78.3XXS (ICDcodes.com, n.d.; ICD10Data, n.d.). Depending on current privileges allowed in Epic, the project team may have to contact the information technology department to allow user permissions for formatting an ICD code list. See Appendix I for instructions in creating a case list by ICD codes in Epic Care Connect.

After one month of guideline implementation, the project team will search for AE cases to assess monitored outcomes. Due to the sporadic nature of AE case presentation, the one-month mark may not be sufficient time to capture any AE cases. To account for the potential variability in AE cases for evaluation, the project team will adjust the monitoring period appropriately, potentially collecting data every two months, or even every six months.

Evaluation of Project Outcomes

Previous clinical trials focused on the following patient outcomes to determine guideline implementation efficacy: mortality, cardiac arrest, anoxic brain injury, time and attempts to definitive airway placement, need for surgical airway, ETT placement complications (bleeding, incorrect placement, cricoid tissue injury), and DAT activation. Biro and Schlaepfer (2018) looked at the number of attempts for successful intubation, as well as the lowest oxygen saturation level registered during intubation. Alvis et al. (2016) likewise tracked time to intubation as well as first pass success rate. Darby et al (2018) tracked DAT activation, ESA placements, cardiac arrest, and patient mortality. In a critical incident database analysis, Cook and MacDougall-Davis (2012) found similar tracking measures across multiple databases. The ASACCP tracks mortality and hypoxic brain injury (Cook & MacDougall-Davis, 2012). Likewise in the United Kingdom, the National Health Service Litigation Authority (NHSLA) tracks airway related deaths and hypoxic brain injuries (Cook & MacDougall-Davis, 2012).

To determine the efficacy of the AE guideline, the project will utilize similar measures as previous studies. The project will look at morbidity/mortality and airway placement data points to determine changes in patient outcomes. Morbidity and mortality data points include patient mortality, hypoxic brain injury, and cardiac arrest. Airway placement metrics include time and attempts to definitive airway securement, and the number of surgical airways. As the project team expects the number of AE cases to be low, a manual chart review and data extraction for the datapoints should be possible by one individual. The project team will process all obtained data points through the Statistical Package for Social Sciences (SPSS) software program, using T tests ($p \leq 0.05$) to compare outcomes prior to and post AE guideline implementation. The project will utilize SPSS software due to ease of use and the project team's familiarity with the software (IBM, n.d.).

After obtaining datapoints from a six to eight-month period, the project team will present findings to hospital administrators and involved departmental leadership. The project team will report de-identified patient data via a Microsoft Teams meeting with a PowerPoint presentation. At that time, the leadership team may ask questions and express concerns or feedback about project outcomes. Direct staff and university representatives will receive disseminated information via a professional poster presentation (the affected hospital staff will receive the poster via workplace email). Again, the project team will be available to answer any questions or concerns via an email format.

If the project shows a successful reduction in patient mortality, time/attempts to definitive airway securement, hypoxic brain injury, and cardiac arrest, the long-term goal is the implementation of the AE guideline and associated trainings in other facilities in the hospital system. The project framework, the Duke University FADE model, promotes project creation as

a pilot basis (B.H.M., n.d.). As such, the next step in a successful project is the transfer of the AE guideline to a larger scale, the hospital system as a whole. Guideline implementation at the remainder of the system facilities will follow a similar implementation plan as utilized in the initial project. If successful, the project hospital should consider repeat ESA training on an annual basis, again with the anesthesia staff and an ENT or trauma surgeon, as the ESA is not frequently performed and annual training may lead to increased provider comfort.

If the project does not improve target measures, the project team will need to consider potential reasons for project failure. Identified potential points of failure fall into two broad categories, implementation barriers or personnel failure. Possible implementation barriers are lack of funding or grants to support the project, lack of buy in from staff and/or administration, and inadequate or improper training (i.e., was the training session not appropriate for staff needs). Additionally, because AE is an unpredictable event and case presentation frequency varies, there may be an insufficient AE caseload to accurately assess project outcomes.

In the personnel realm, the largest potential point of failure is not following the guideline and continuing previous, status quo AE management. Not following the AE guideline may lead to continued delay in recognition of AE and calling for help, ED providers attempting airway interventions, continued use of inappropriate intubation methods (direct laryngoscopy) and a reluctance or delay in attempting a surgical airway. Staff turnover, both in the ED and anesthesia departments could also result in inadequate outcomes, as the new staff may not receive the same guideline, AEC, and ESA training.

Conclusion

AE accounts for more than one million visits to the ED each year in the United States, with frequency and resulting hospitalizations only increasing (Bernstein et al., 2017). Therefore,

the development of a clear, evidence-based method of treating AE is imperative both for hospital efficiency and patient safety. The most comprehensive method to ensure optimal AE management is the creation of a multidepartmental AE guideline for hospital wide implementation. Implementation of an AE guideline requires buy in from multiple departments throughout the facility, such as ED, anesthesia, and pharmacy. All stakeholders must feel heard and receive reassurance they are valued members of the team (Mason et al., 2021).

The proposed AE guideline covers aspects of AE management, including initial assessment, medical management and airway techniques. Creation of an AE guideline allows for increased team building and comfort in knowing individual job roles. The guideline presents the expectations for each department as well as identifies appropriate medications and airway interventions based on updated evidence-based practice. Although implementation appears costly at first glance, providing clear, delineated guidance for AE care leads to a reduction in invasive airways needed (and thus longer ICU stays), decreased patient morbidity and mortality, and decreased hospital expenses. By working together as a cohesive team, members work together to ensure the ultimate patient goal – safety.

References

Alternative Source Medical. (2022). *Olympus BF-160 video bronchoscope - refurbished*. Alternative Source Medical. Retrieved March 31, 2022, from https://altsourcemedical.com/products/olympus-bf-160-video-bronchoscope-refurbished?variant=13259792580652&utm_campaign=gs-2018-07-26&utm_source=google&utm_medium=smart_campaign&gclid=CjwKCAjwopWSBhB6EiwAjxmqDfwdQCS-qZkBa9pNbMPTlWFDnyS2LsHpr4KefKXHNDvAUGKZ7s5IxhoCpeYQAvD_BwE

Alvis BD, Hester D, Watson D, Higgins M, St Jacques P. Randomized controlled trial comparing the McGrath MAC video laryngoscope with the King Vision video laryngoscope in adult patients. Minerva Anesthesiology. 2016; 82: 30-35

Ahmad I (2017). Regional and topical anesthesia for awake endotracheal intubation. Hadzic A(Ed.), *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management, 2e*. McGraw Hill. https://accessanesthesiology.mhmedical.com/content.aspx?bookid=2070&sectionid=157600034

Anesthesiologist salary. Zip Recruiter. (2022). Retrieved August 24, 2022, from https://www.ziprecruiter.com/Salaries/Anesthesiologist-Salary

Bernstein, J. A., Moellman, J. J., Collins, S. P., Hart, K. W., & Lindsell, C. J. (2015). Effectiveness of ecallantide in treating angiotensin-converting enzyme inhibitor–induced angioedema in the emergency department. *Annals of Allergy, Asthma & Immunology*, *114*, 245–249. https://doi.org/10.1016/j.anai.2014.12.007

Bernstein, J. A., Cremonesi, P., Hoffmann, T. K., & Hollingsworth, J. (2017). Angioedema in the emergency department: A practical guide to differential diagnosis and management. *International Journal of Emergency Medicine*, *10*(15), 1–11. https://doi.org/10.1186/s12245-017-0141-z

BHM Marketing. (n.d.). *The drive for healthcare quality and pay for performance*. BHM Healthcare Solutions. Retrieved May 31, 2022, from https://bhmpc.com/2014/01/drive-healthcare-quality-pay-performance/

Biro, P., & Schlaepfer, M. (2018). Tracheal intubation with channeled vs. non-channeled videolaryngoscope blades. *Romanian Journal of Anaesthesia and Intensive Care*, *25*(2), 97–101. https://doi.org/10.21454/rjaic.7518.252.sch

Bohrer, K. (2012). Emergent treatment of angioedema. *The International Student Journal of Nurse Anesthesia*, *11*(2), 19–22.

Bowen, T., Cicardi, M., Farkas, H., Bork, K., Longhurst, H., Zuraw, B., Aygoeren-Pursun, E., Craig, T., Binkley, K., Herbert, J., Ritchie, B., Bouillet, L., Betschel, S., Cogar, D., Dean, J., Devaraj, R., Hamed, A., Kamra, P., Keith, P., … Xiang, Z. Y. (2010). 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy, Asthma & Clinical Immunology*, *6*(24), 1–13. https://doi.org/10.1186/1710-1492-6-13

Brambrink, A. M., & Hagberg, C. A. (2013). The ASA difficult airway algorithm: Analysis and presentation of a new algorithm. In C. A. Hagberg (Ed.), *Benumof and Hagberg's Airway Management* (3rd ed., pp. 222–239). essay, Elsevier/Saunders.

Brown, T., Gonzales, J., & Monteleone, C. (2017). Angiotensin-converting enzyme inhibitor-induced angioedema: A review of the literature. *Journal of Clinical Hypertension, 19,* 1377–1382. https://doi.org/10.1111/jch.13097

BSN annual salary. Zip Recruiter. (2022). Retrieved August 22, 2022, from https://www.ziprecruiter.com/Salaries/BSN-Salary

Cappellino, A. (2021, August 25). *Medical malpractice payout report for 2018*. Expert Institute. Retrieved August 24, 2022, from https://www.expertinstitute.com/resources/insights/medical-malpractice-payout-report-for-2018/

Cicardi, M., Bellis, P., Bertazzoni, G., Cancian, M., Chiesa, M., Cremonesi, P., Marino, P., Montano, N., Morselli, C., Ottaviani, F., Perricone, R., Triggiani, M., & Zanichelli, A. (2014). Guidance for diagnosis and treatment of acute angioedema in the emergency department: Consensus statement by a panel of Italian experts. *Internal and Emergency Medicine, 9*(1), 85–92. https://doi.org/10.1007/s11739-013-0993-z

Conroy, R. M. (2018, May). *The RCSI Sample Size Handbook*. RCSI Data Science Centre Guides. Retrieved October 12, 2022, from https://www.researchgate.net/publication/324571619_The_RCSI_Sample_size_handbook Affiliation: Royal College of Surgeons in Ireland. DOI: 10.13140/RG.2.2.30497.51043

Cook, T. M., & MacDougall-Davis, S. R. (2012). Complications and failure of airway management. *British Journal of Anaesthesia*, *109*, i68–i85. https://doi.org/10.1093/bja/aes393

CRNA annual salary in Ohio. Zip Recuiter. (2022). Retrieved August 22, 2022, from https://www.ziprecruiter.com/Salaries/CRNA-Salary--in-Ohio

Darby, J. M., Halenda, G., Chou, C., Quinlan, J. J., Alarcon, L. H., & Simmons, R. L. (2018). Emergency surgical airways following activation of a difficult airway management team in hospitalized critically ill patients: A case series. *Journal of Intensive Care Medicine*, *33*(9), 517–526. https://doi.org/10.1177/0885066616680594

Dasta, J. F., McLaughlin, T. P., Mody, S. H., & Piech, C. T. (2005). Daily cost of an intensive care unit day: the contribution of mechanical ventilation. *Critical care medicine*, *33*(6), 1266–1271. https://doi.org/10.1097/01.ccm.0000164543.14619.00

Driver, B. E., & McGill, J. W. (2017). Emergency department airway management of severe angioedema: A video review of 45 intubations. *Annals of Emergency Medicine*, *69*(5), 635–639. https://doi.org/10.1016/j.annemergmed.2016.11.027

EBSCOhost Research Platform: EBSCO. EBSCO Information Services, Inc. | www.ebsco.com. (2022). Retrieved June 7, 2022, from https://www.ebsco.com/products/ebscohost-research-platform

Emergency medicine physician salary. Zip Recruiter. (2022). Retrieved August 24, 2022, from https://www.ziprecruiter.com/Salaries/Emergency-Medicine-Physician-Salary

Fisher, D., & Abukhdeir,, H. (2016, December 1). *Understanding and managing angioedema in the emergency department*. Emergency Medical Reports. Retrieved June 14, 2022, from https://www.reliasmedia.com/articles/139671-understanding-and-managing-angioedema-in-the-emergency-department

Frerk, C., Mitchell, V. S., McNarry, A. F., Mendonca, C., Bhagrath, R., Patel, A., O'Sullivan, E. P., Woodall, N. M., & Ahmad, I. (2015). Difficult airway society 2015 guidelines for management of unanticipated difficult intubation in adults. *British Journal of Anaesthesia*, *115*(6), 827–848. https://doi.org/10.1093/bja/aev371

Gil, K. S. L., & Diemunsch, P. A. (2013). Fiberoptic and flexible endoscopic-aided techniques. In C. Hagberg (Ed.), *Hagberg and Benumof's Airway Management* (pp. 365–411). essay, Elsevier.

Global Equipment Company. (2022). *Detecto® Rescue Series General Purpose Medical Cart, white frame with 5 white drawers*. Global Industrial. Retrieved March 31, 2022, from https://www.globalindustrial.com/p/rescue-series-general-purpose-medical-cart-white-frame-with-5-white-drawers?infoParam.campaignId=T9F&gclid=CjwKCAjwopWSBhB6EiwAjxmqDdlW3OPrHiIqAV7QA1FtcGWSwtkHpCSHL4QwGOxzA22FZcps18OkHxoClx0QAvD_BwE

Gonzalez, M. N., Weston, B., Yuce, T. K., Carey, A. M., Barnette, R. E., Goldberg, A., & McNamara, R. M. (2016). One-year experience with the institution of a critical airway team at an academic medical center. *The Journal of Emergency Medicine*, *50*(1), 194–197. https://doi.org/10.1016/j.jemermed.2015.09.011

Greve, J., Bas, M., Hoffmann, T. K., Schuler, P. J., Weller, P., Kojda, G., & Strassen, U. (2015). Effect of C1-esterase-inhibitor in angiotensin-converting enzyme inhibitor-induced angioedema. *The Laryngoscope*, *125*(6), E198–E202. https://doi.org/10.1002/lary.25113

GSK plc. (2018). *Creating a patient list for asthma or COPD patients in Epic EHR*. GSK plc. Retrieved October 12, 2022, from https://gskpro.com/content/dam/global/hcpportal/en_US/pdf/ehr-resources/asthma-copd-patient-list-nextgen-ehr.pdf

GTSimulators. (2022). *Bronchoscopy model - broncho boy*. Bronchoscopy model - Broncho boy. Retrieved March 31, 2022, from https://www.gtsimulators.com/products/bronchoscopy-model-broncho-boy-cla9?variant=36901645713557#BeginDescription

GT Simulators. (2022). *Cricothyrotomy Simulator*. GTSimulators.com. Retrieved March 31, 2022, from https://www.gtsimulators.com/products/cricothyrotomy-simulator-lf00994u

GTSimulators. (2022). *Difficult airway management simulator*. Difficult Airway Management Simulator. Retrieved March 31, 2022, from https://www.gtsimulators.com/collections/airway-management-training/products/difficult-airway-management-simulator-kk-mw13

Heard, A. M., Green, R. J., & Eakins, P. (2009). The formulation and introduction of a ‘can't intubate, can't ventilate’ algorithm into clinical practice. *Anaesthesia*, *64*(6), 601–608. https://doi.org/10.1111/j.1365-2044.2009.05888.x

IBM. (n.d.). *SPSS statistics - overview*. IBM SPSS Statistics. Retrieved October 12, 2022, from https://www.ibm.com/products/spss-statistics

ICD9Data. (n.d.). *2012 ICD-9-CM Diagnosis Code 995.1 : Angioneurotic edema, not elsewhere classified*. 2012 ICD-9-CM Diagnosis Code 995.1. Retrieved September 2, 2022, from http://www.icd9data.com/2012/Volume1/800-999/990-995/995/995.1.htm

ICD10Data. (n.d.). *2022 ICD-10-CM diagnosis code T78.3XXA*. ICD10Data.com. Retrieved September 2, 2022, from https://www.icd10data.com/ICD10CM/Codes/S00-T88/T66-T78/T78-/T78.3XXA

ICDcodes.com. (n.d.). *Angioneurotic edema T78.3*. ICDCodes.com Clinical Database. Retrieved September 2, 2022, from https://icd-codes.com/icd10cm/S00-T88/T66-T78/T78/T78.3

Jaiganesh, T., Hughan, C., Webster, A., & Bethune, C. (2012). Hereditary angioedema. *European Journal of Emergency Medicine*, *19*(4), 271–274. https://doi.org/10.1097/mej.0b013e32834c9e1f

Jaiganesh, T., Wiese, M., Hollingsworth, J., Hughan, C., Kamara, M., Wood, P., & Bethune, C. (2013). Acute angioedema: Recognition and management in the emergency department. *European Journal of Emergency Medicine*, *20*(1), 10–17. https://doi.org/10.1097/MEJ.0b013e328356f76e

Jordan, L., Quraish, J., & Liao, J. (2013). The National Practitioner Data Bank and CRNA anesthesia related malpractice payments. *AANA Journal*, *81*(3), 178–182.

Kang FG, Kendall MC, Kang JS, Malgieri CJ, De Oliveira GS. Medical Malpractice Lawsuits Involving Anesthesiology Residents: An Analysis of the National Westlaw Database. J Educ Perioper Med. 2020 Oct 1;22(4):E650. doi: 10.46374/volxxii-issue4-deoliveira. PMID: 33447649; PMCID: PMC7792582.

Kelly, M., Donnelly, J. P., McAnnally, J.-R., & Wang, H. E. (2013). National estimates of emergency department visits for angioedema and allergic reactions in the United States. *Allergy and Asthma Proceedings*, *34*(2), 150–154. https://doi.org/10.2500/aap.2013.34.3640

King Vision™ led video laryngoscope kit: Bound Tree. King Vision™ LED Video Laryngoscope Kit | Bound Tree. (n.d.). Retrieved October 7, 2022, from https://www.boundtree.com/airway-oxygen-delivery/video-laryngoscopes/king-vision-led-video-laryngoscope-kit/p/2144-KV311

Lee, S. K., Rosenthal, A., Davare, D. L., Kiffin, C., Sanchez, R., Hurtado, M., & Carrillo, E. H. (2017). Inclusion of the acute care surgeon in the difficult airway protocol: A nine-Year experience. *The American Surgeon*, *83*(9), 943–946. https://doi.org/10.1177/000313481708300929

Lewis, L., Graffeo, C., Crosley, P., Klausner, H. A., Clark, C. L., Frank, A., Miner, J., Iarrobino, R., & Chyung, Y. (2015). Ecallantide for the acute treatment of angiotensin converting enzyme inhibitor-induced angioedema: A multicenter randomized controlled trial. *Annals of Emergency Medicine*, *65*(2), 204–213. https://doi.org/10.1016/j.annemergmed.2013.07.197

Long, B., Koyfman, A., & Gottlieb, M. (2019). Evaluation and management of Angioedema in the emergency department. *Western Journal of Emergency Medicine*, *20*(4), 587–595. https://doi.org/10.5811/westjem.2019.5.42650

Maurer, M., Magerl, M., Ansotegui, I., Aygören-Pürsün, E., Betschel, S., Bork, K., Bowen, T., Balle Boysen, H., Farkas, H., Grumach, A. S., Hide, M., Katelaris, C., Lockey, R., Longhurst, H., Lumry, W. R., Martinez-Saguer, I., Moldovan, D., Nast, A., Pawankar, R., … Craig, T. (2018). The international WAO/EAACI guideline for the management of hereditary angioedema-the 2017 revision and update. *Allergy*, *73*(8), 1575–1596. https://doi.org/10.1111/all.13384

Melnyk, B. M., & Fineout-Overhalt, E. (2019). *Evidence based Practice in Nursing and Healthcare* (4th ed.). Wolters Kluwer.

Misra, L., Trentman, T., & Khurmi, N. (2016). Angioedema: Classification, management and emerging therapies for the perioperative physician. *Indian Journal of Anaesthesia*, *60*(8), 534–540. https://doi.org/10.4103/0019-5049.187776

Moran, K. J., Burson, R., & Conrad, D. (2020). *The doctor of nursing practice project: A framework for success*. Jones & Bartlett Learning.

Nilsen, P. (2015). Making sense of implementation theories, models and frameworks. *Implementation Science*, *10*, 1–13. https://doi.org/10.1186/s13012-015-0242-0

OhioHealth. (2022). *Out-of-pocket estimates and pricing: OhioHealth*. OhioHealth.com. Retrieved April 3, 2022, from https://www.ohiohealth.com/patients-and-visitors/prepare-for-your-visit/price-estimator

Otani, I. M., Christiansen, S. C., Busse, P., Camargo, C. A., Zuraw, B. L., Riedl, M. A., & Banerji, A. (2017). Emergency department management of hereditary angioedema attacks: Patient perspectives. *The Journal of Allergy and Clinical Immunology: In Practice*, *5*(1), 128–134. https://doi.org/10.1016/j.jaip.2016.06.029

Otolaryngologist salary. Zip Recruiter. (2022). Retrieved August 22, 2022, from https://www.ziprecruiter.com/Salaries/Otolaryngologist-Salary

Pandian, V., Zhen, G., Stanley, S., Oldsman, M., Haut, E., Mark, L., Miller, C., & Hillel, A. (2019). Management of difficult airway among patients with oropharyngeal angioedema. *The Laryngoscope*, *129*(6), 1360–1367. https://doi.org/10.1002/lary.27622

Parkey, S., Erickson, T., Hayden, E. M., Brown III, C. A., & Carlson, J. N. (2019). Flexible nasotracheal intubation compared to blind nasotracheal intubation in the setting of simulated angioedema. *The American Journal of Emergency Medicine*, *37*, 1995–1998. https://doi.org/10.1016/j.ajem.2019.02.012

Popovici, S. E., & Mitre, C. (2018). Difficult airway management – A constant challenge. *Romanian Journal of Anaesthesia and Intensive Care*, *25*(2), 93–94. https://doi.org/10.21454/rjaic.7518.252.pop

Rai, M. R., Amen, F., & Idrees, F. (2004). Angiotensin-converting enzyme inhibitor related angioedema and the Anaesthetist. *Anaesthesia*, *59*(3), 283–289. https://doi.org/10.1111/j.1365-2044.2004.03614.x

Rajan, N., Sharma, V., Patro, S. K., & Goyal, A. (2020). Acute presentation of undiagnosed hereditary angioedema of the larynx: Averting death. *Turkish Archives of Otorhinolaryngology*, *58*(4), 279–281. https://doi.org/10.5152/tao.2020.5994

Rosi-Schumacher, M., Shah, S. J., Craig, T., & Goyal, N. (2021). Clinical manifestations of hereditary angioedema and a systematic review of treatment options. *Laryngoscope Investigative Otolaryngology*, *6*(3), 394–403. https://doi.org/10.1002/lio2.555

Saeb, A., Hagglund, K. H., & Cigolle, C. T. (2016). Using fresh frozen plasma for acute airway angioedema to prevent intubation in the emergency department: A retrospective cohort study. *Emergency Medicine International*, *2016*, 1–6. https://doi.org/10.1155/2016/6091510

Sandefur, B. J., Liu, X.-W., Kaji, A. H., Campbell, R. L., Driver, B. E., Walls, R. M., Carlson, J. N., & Brown, C. A. (2021). Emergency department intubations in patients with angioedema: A report from the National Emergency Airway Registry. *The Journal of Emergency Medicine*, *61*(5), 481–488. https://doi.org/10.1016/j.jemermed.2021.07.012

Trauma surgeon annual salary. Zip Recuiter. (2022). Retrieved August 22, 2022, from https://www.ziprecruiter.com/Salaries/Trauma-Surgeon-Salary

U. S. Department of Health and Human Services Health Resources and Services Administration. (2011). *Quality improvement - Health Resources and Services Administration*. Quality Improvement. Retrieved May 31, 2022, from https://www.hrsa.gov/sites/default/files/quality/toolbox/pdfs/qualityimprovement.pdf

Vuzitas, A., & Sarafoleanu, C. (2016). Hereditary angioedema - An otolaryngologist's perspective. *Romanian Journal of Rhinology*, *6*(23), 133–138. https://doi.org/10.1515/rjr-2016-0015

Walsh, R. M., Cookman, L., & Luerssen, E. (2014). Comparison of intubation performance by emergency medicine residents using gum elastic bougie versus standard stylet in simulated easy and difficult intubation scenarios. *Emergency Medicine Australasia, 26*, 446–449. https://doi.org/10.101111/1742-6723.12280

Wiseman, B., & Kaprielian, V. (2021). *FADE*. What is quality improvement? Retrieved May 31, 2022, from https://josieking.org/patientsafety/module_a/methods/fade.html

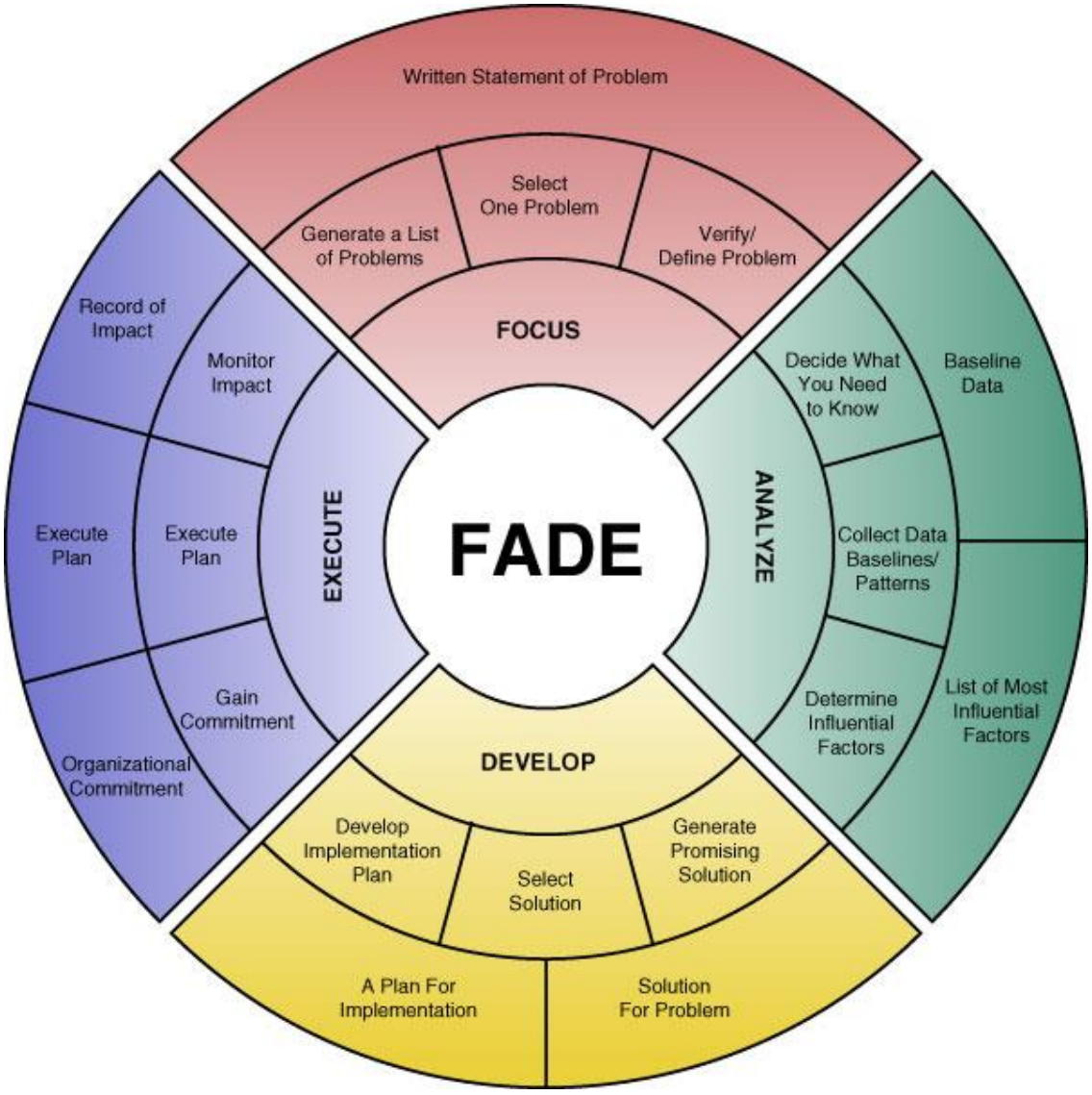
Wood, A., Choromanski, D., & Orlewicz, M. (2013). Intubation of patients with angioedema: A retrospective study of different methods over three year period. *International Journal of Critical Illness and Injury Science, 3*(2), 108–111. https://doi.org/10.4103/2229-5151.114267

Yeung, E. K., Saikumar, H., Castaneda-Nerio, J., Adams, S. G., & Wong, M. (2018). Icatibant for angiotensin-converting enzyme inhibitor-induced angioedema in intubated patients: Case series and literature review. *Case Reports in Critical Care, 2018*, 1–6. https://doi.org/10.1155/2018/8081607

Zuraw, B., Busse, P., White, M., Jacobs, J., & Lumry, W. (2010). Nanofiltered C1 inhibitor concentrate for treatment of hereditary angioedema. *The New England Journal of Medicine, 363*(6), 513–522. https://doi.org/10.1056/NEJMoa0805538

Appendix A

Duke University FADE Model for Quality Improvement



Note. From *What is Quality Improvement*, by Wiseman, B. and Kaprielian, V., 2021, Josie King Foundation and Duke University School of Medicine (https://josieking.org/patientsafety/module_a/methods/fade.html). Patient Safety module series used with permission from Duke University © Duke University 2002-2022

Appendix B

Permissive Use of FADE Model by Duke University

NON-EXCLUSIVE LICENSE

Megan A. Przybysz

Otterbein University, College of Nursing

1 S. Grove St Westerville, OH 73081

przybysz1@otterbein.edu

Duke University

Department of Family Medicine and Community Health DUMC 2914

2200 W. Main St.

Erwin Square, 4th Floor, Suite 420

Durham, NC 27710

(919) 681-3178

Duke University (“Duke”) hereby grants Megan A. Przybysz (“Licensee”) the non-exclusive right to reproduce, incorporate, and/or distribute the work described below (the “Work”), in whole or in part without alteration of the content, in connection with Licensee’s doctoral dissertation at Otterbein University (the “Project”), in future revisions, remakes, distributions, and promotional materials thereof, including non-exclusive world rights in all languages and media, and to the prospective publication of the Project by Digication. These rights will in no way restrict the use and republication of Duke's material in any form by Duke, or those authorized by Duke.

Appendix B (Cont.) Permissive Use of FADE Model by Duke University

For the purposes of this license the "Work" is defined as the Patient Safety module series by Beau Wiseman and Victoria Kaprielian contained on the Josie King Foundation website. The module series is an online program that was created to introduce clinical faculty and trainees to fundamental concepts of patient safety and quality improvement. It is intended as an efficient means of asynchronously providing foundational content to busy clinicians and trainees, as part of larger quality and safety initiatives.

Duke is the owner of all copyrights in the Work and has full authority to grant this license. As consideration for this license, Licensee will use the following credit line -***Patient Safety module series used with permission from Duke University*** -and the following copyright notice -© ***Duke University 2002- [current year]-*** in the Project.

Licensee may use the Work only for noncommercial purposes and Licensee may not sell, transfer, license or otherwise distribute the Work except as specified above. Licensee may terminate the license at any time and without notice to Duke by stopping all use of the Work. Duke may terminate the license in the event Licensee is in default of the obligations under this license and fails to remedy any such default within sixty (60) days of receipt of written notice from Duke. The laws of the state of North Carolina shall govern this license. In the event any dispute arising in relation to this license results in litigation, arbitration or mediation, such action or proceeding shall be brought only within the state or federal courts of Durham County, North Carolina.

Appendix B (Cont.) Permissive Use of FADE Model by Duke University

Duke grants permission for the use requested above effective as of the execution date of this letter as noted below.

Duke University

By: 

[Name] Anthony Viera

[Title] Department Chair

Date: 9/8/22

Appendix C

Literature Review Level of Evidence Table

Authors	Date	Level of Evidence	I.Systematic review/ meta-analysis of RCT	II. Single RCT	III.Nonrandomized control trial	IV. Cohort/ case control study	V. Metasynthesis of qualitative study	VI. EBP/ QI /	VII. Expert Opinion
Misra et al	2016		x						
Caballero et al	2011								x
otani et al	2016							x	
Parkey et al	2019			x					
Karadza-Lapic et al	2017				x				
wood et al	2013					retroactive			
Pandian et al	2019					retro			
Walsh et al	2014			x					
Driver et al	2017					retro			
Bowen Et al	2010								x
Maurer et al	2017								x
heard et al	2009				x				
Moellman et al	2014								x
Rosenbaum et al	2021		x						
Long et al	2019		x						
Bernterin et al	2017								x
Yeung et al	2018					x			
Rosi Schumacher	2020		x						
Brown et al	2017		x??						
Cook &MacDougall-Douglas	2012							x	
Gonzalez et al	2015					retroactive x			
Darby et al.	2018							x	
Lee et al	2017					retro			
Jaiganesh et al.	2012							x	
Jaiganesh	2013								x
Bernstein et el	2015			x					
Greve et al.	2015					retro			
Zuraw et al	2010			x					

Appendix D

Literature Review Outcome Summary Table

Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Mistra et al	2016	1	Meta-analysis			Database search for terms: hereditary angioedema, aquired angioedema, icatibant, ecallantide, C1 esterase inhibitor	Pubmed, medline, embase, scopus, web of science database	MC v BK AE is different tx. Tx all as Anaphylaxis to start; for BK AE, tx with Icatibant, Ecallantide, and C1 INH (no preference given btwn drugs)	no preference given between the 3 listed drugs or results as far as effectiveness, Only disucss that FFP has fallen out of favor	
Caballero et al	2011	7	Expert opinion			review of scienific papers on different types of BK induced AE	English language Pubmed search: AE, BK, HAE, acquired angioedema, C1 inhibitor deficiency, estrogens, HAE type III, HAE-FX II, angiotensin 1 converting enzyme inhibitors	Discussed differences between BK AE	Very detailed content on detailed types of BK AE but not a lot on treatments; wasn't exactly helpful/useful	Consensus statement from the "Spanish study group on BK induced AE"
Otani et al	2016	6	Descriptive Study	105		pts with HAE completed a questionairre about HAE mgmt in the ED	pts with HAE who attended HAE pt summit in 2015	99% pts said ED needs better understanding of HAE (recongition of HAE dx, severity and med mgmt) Having an HAE tx plan in place greatly increased liklihood of correct tx; even with tx plan in place or presence of ED	this does not provide a lof of data. Is more pt perspectives with some statistics thrown in.	Based on subjective opinions ; population bias
Yeung et al	2018	4	retrospective analysis	3		Pubmed & Medline search for case reports	Pubmed & Medline search for case reports; terms: icatibant, angiotensin converting enzyme induced angioedema, intubation	pt's did not improve rapidly. Onset of improvemetn at 11-22hrs and remained intubated 3-5 days post med admin	small study size. Only used pts already intubated; pts did not receive icatibant until 11+ hrs after arrival; pts received other treatments	use of Icatibant for off label use (ACEi AE)
Schumacher et al	2020	1	Metanalyis	55 articles		Pubmed, Embase database from start of database to Feb 2021	included systematic reviews, RCT, prospective/retrospective cohort studies and outcomes research	discussed acute and long term phophylaxis (not utilized) meds	parts of the apper irrelevant. No real research done	Written from an otolaryngoloist standpoint; can also use this in the formulation section
Brown et al	2017	1; unsure. Lit review	Metanalyisis-unsure. Lit	unsure. No total given		Pubmed	terms "ACE'I and "AE"	backgound/ patho of AE, medication manamement; focus on ACEi AE	does not list sources for studies, unsure if gathered from peer reviewed journals.	good for basic data, but leaves a lot of questions as far as data source and if the studies referenced are actually good studies

Appendix D (Cont.)

Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Parkey et al	2019	3	Non blind Single Non RCT	20	People may have tried both, so not really	Sim-man with AE. Blling NTT/FOB with parker tube; given 10min presentation on FOB and 10 min play w/o Sim; whistle recording played for blind, palcement confimred by BVM	Observation, researcher timing, chest rise with BVM	TTI blind and FOB not sign different; but bigger time difference (FOB longer) in Jr providers (FOB only 50% 1st pass success per NEAR database?)	used manequin, not real person. Used med students to senior proivders, so varying levels of skills. ED providers, not anesthesia.	Not evereyone familiar with tools used and not a lot of time given to try materials. Only used one type NTT. Blnid ETT sounds simulated
Karadza-Lapic et al	2017	4	Retroactive case control	15		EMR modified to ID pts with HAE and info on how to tx, contact info for specalist MD, NOK, warning no ACEi or oral BC pills; also pt edu on condition and medical ID card with HAE info; Infor on HAE sent to kids schools	EMR review; 3 pts of 15 visited ED for HAE in study time period. Total of 12 HAE attacks	pts still not reporting HAE dx to providers consistently, but all who went to hospital for things did. However, AE still missed (so mistreated) Correct therapy given more often (p.0.006) and prophlacic meds given more	Doesn't really address HOW they edu pts. If stressed importance of telling providers?	HAE still often misdx, leading to unnecssary cost/tx and pts still not aware of importance of notifying ALL providers of dx. Makes EMR flag even more important
Wood et al	2013	4	Retroactive case control	33	FOB:12, VL:11, Other:10	pts 18-80 w/ AE dx and compromised airway	retrospective chart review from one hospital using "emergency intubation" or "emer trach." Measured # attempts, time to success (from IV meds to EtCO2)	VL/other sign shorter than FOB, no difference in 1st pass success; TTI VL 6.9min, TTI FOB 10.4min 1st pass FOB 83.3%, VL100%, O 70%	Small sample size; mult MDA; no grade scale on severity of AE; only used OR cases, not ED;	All MDA. 10 attendings with 3+ years experience, all experience with glidescope; "Other" is DL, intubating LMA(LMA not recommended, AE preents secure seal) and blind nasal; Glidescope gives "macroview" of airway vs FOB VL more efficient method! Fast/safe airway = less risk hypoxic arrest; admit VL may not be possible 2/2 amount of swelling; other injuries from glidescope; FOB proficiency =more time/skill

Appendix D (Cont.)

Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Pandian et al	2019	4	Retroactive case control	63	36 PreDART, 27 PostDART	Created Difficult airway team (DART) (multidiscipline) and cart; implemented mass team page for difficult airway (Otolaryngologist on team)	Chart review from one facility. Divided into 5 years pre and 5 post implementation; included AE pts severe enough for specalists or airway intervention	PreDART 77% from the ED. Post Dart 55% (ICU went up) no diff in age/gender; Time to respond Pre: 89.2min, Post 3.36 min FOB from 56% to 82%, less pts needed OR for airway post DART	Large diff in AE causes in Pre/post DART; retroactive study; did not have strict criteria on when to secure airway; admitted not best record keeping in pre DART era, may have missed cases	both had 1 emerg cric. Pre DART ED tried a lot B4 calling for help and pt deteriated, post DART, called for help early
Walsh et al	2014	3	Non RCT	29	29 (all did both) randomized to who got what view first	Cadaver sniffing=grade I; C-collar = grade 3; 7.5ETT Mac 4 blade via DL; >300 seconds attempt =failed intubation	Time from "begin" command to inflation of ETT balloon; timed by researcher, placement verified by researcher and glidescope	TTI longer with GEB than ETT-S in Grade 3 view, but more successful (trend, not stat sign), no real time diff in grade 1 view; TTI Grade 1 46.3sec, Grade 3 77.6sec; diff of 40.9 sec in Grade 3 with GEB longer	used ED PGY1 students, less experience with ETT in general; 116 total intubations but 36% were "failed"	Should have variety of provider experience (45% PGY1, 31 PGY2, 24% PGY3) 69% completed anesthesia roation as med student, 59% as a resident; even with GEB Grade 3, only 55% success rate (was 35% with ETT-S)
Driver Et al	2017	4	Retroactive Case control	45		TTI: blade into mouth until removal (fail) or EtCO2	Retroactive review of AE intubation videos in one ED (L1trauma); resucs room tapes; 2 reserches independ reviewed the videos for data	VL greatest % success(86%) compared to FOB nasal (55) and FOB oral (67) Blind nasal (40) TTI VL 44sec, FOBN 385sec, FOBO 125sec; VL/DL higher success for first pass attempt vs rescue.	Unable to determine severity of AE in each case. Wall camera do not catch, no consistency on recirding via FOB; an "attempt" was just per device/intervention., regardless of manipulations with that type; not considered esoph intub if no BVM given; median TTI is 7 min!	GEB was used for all DL/VL with mac blade; No AE/diff airway protocol in place at facility; usu PGY3 doing ETT; 2 pts required more invasive airways after faild FOBN, DL/VL attempts; "intubation duration may correlate better with complications than the number of attempts"

Appendix D (Cont.)

Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Bowen Et al	2010	7	Expert			claim to eval outcomes based on phase III and IV drug trials	Various Canadian medical networks evaluated existing studies/data	Address diagnosis, labs, prophylatic & acute HAE tx, with creation of prophylactic algorithm	focus is on prophylactic mgmt of AE, not acute attacks; Expert opinion; don't really state where data came from	only for HAE (but can extrapolate to all BK AE)
Maurer et al	2018	7	expert			"working groups assigned to eval the data"	"international expert panel reviewed existing evidence"	20 recommendations developed	A lot of the focus is on prophylactic mgmt of AE, not acute attacks; all just expert opinion	only for HAE (but can extrapolate to all BK AE)
Heard et al	2009	3	Non RCT	60	10	1hr sim edu on tech, then session on sheep; difficult airway created by instilling fluid into exterior neck, so can't palpate landmarks. 5 attempts blind and if can't find, then can dissect neck to find trachea; poceudre starts when O2 sats 70% and failed at 4min	Timed from when start to 1st effective vent	Scalp boug: 100%, 39sec Sugical Cric: 80%, 61 sec Melker Cric Kit: 90%, 118sec Mini-trach II: 90%, 163sec Needle: 40%, 106 sec Scalp/finger: 100%, 86 sec	Study conducted on SHEEP!	Surgeon will be better with a scalpel, Anesthes will be better with a cannula - suggest maybe different diff airway alg for diff provers (this seems messy)
Moellman et al	2014	7	expert			PubMed, Google Scholar, Chochran	Allergists and emergency providers	FOB use for intubation. Seems not as aggressive with intubation; recommends FFP as only reliable tx	Expert opinion things missed? Tables/recommnedations written in harder to follow format	mostly focuses on the types of AE; treatments methods that ARE mentioned contradict the other articles
Rosenbaum et al	2021	1	Meta analysis	46 final papers		PubMed 2012-2019	clinical practice committee American academy Em. Med	Primary AE mgmt focus = airway mgmt; no specific medication tx recommended	no tx recommendations	referenced studies utilized. Need to look and see if any relevant to project
Long et al	2019	1	Meta analysis	185 articles		Pubmed, google scholar				

Appendix D (Cont.)

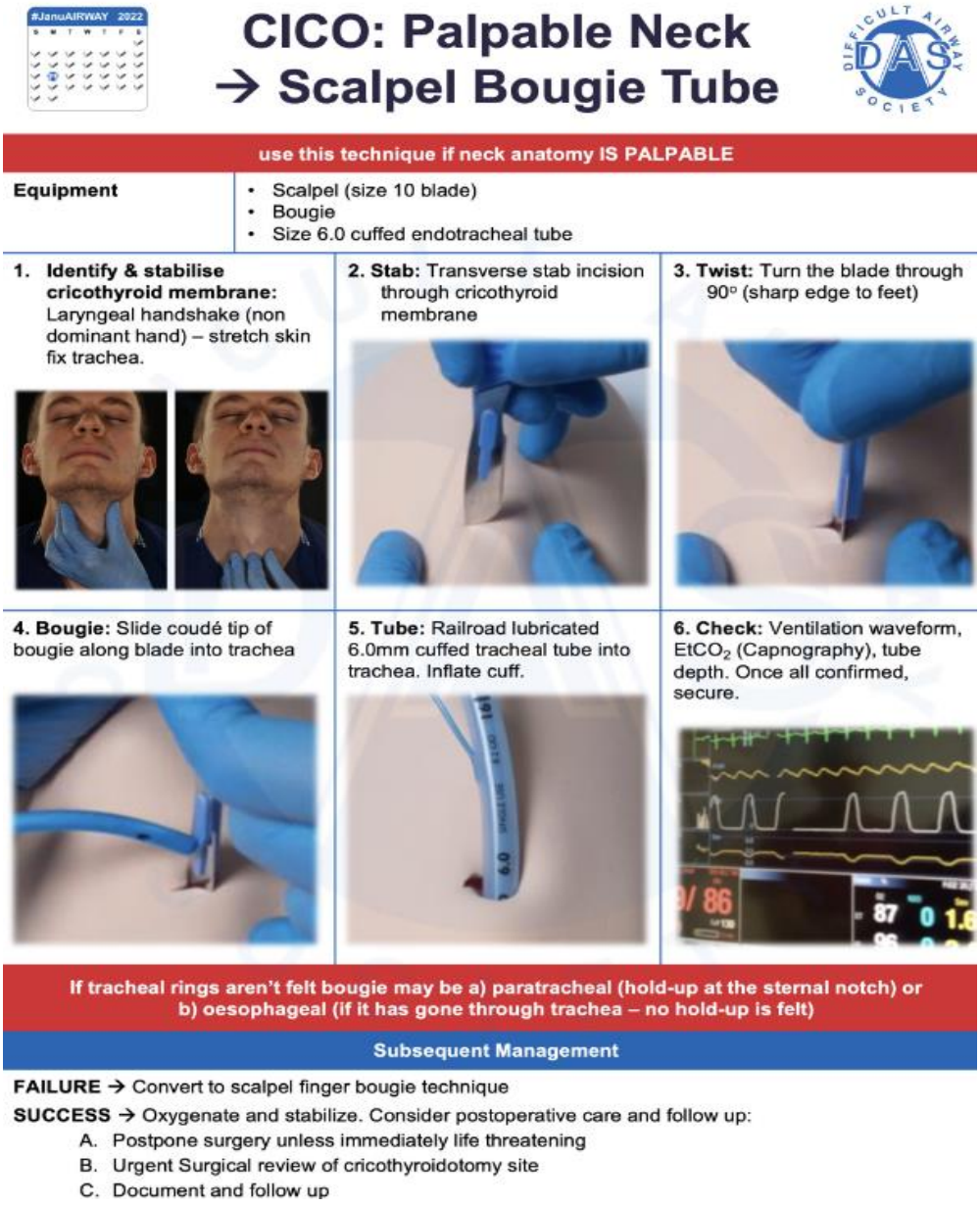
Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Bernstein et al	2017	7	Expert				2 expert panels of 16 international experts in AE from 2013	missing protocols and unavail medications = delay/mistakes of care	No real results b/c is just expert opinion	no recommendations given re medication use.
Cook &Mac Dougall-Douglas	2012	6	EBP/Descriptive Study				closed claims databases, litigation datasets from trhe USA, Canada, UK, Denmark			
Gonzalez et al	2015	4	Retroactive Case control	51; 20/41% AE cases	0	Review of CAT activations over a one year period	retrospective chart review	51 activations; FOB use most common, one surgical airway, no adverse outcomes	does not address things like response times, time/attempts to definitive airway. No control group	Only real measurement is "adverse outcomes" but does not define this
Darby et al.	2018	7	QI project	207 activations; 22 ESA	0	cric or trach pts included (excep	retrospective chart review of pts getting ESA; continued to look at outcomes 2yrs after iniital 1 year look. Found continued decrese in ESA/mortality	early ID of difficult airway and Team mgmt may reduce negative outcomes	DA often placed in OR. This study excluded them; also excludes ESA in OR/ED	Good list of what was in their DA bag
Lee et al	2017	4	retrospecive case control	43 (9 Al	0	Eval survival d/c and ESA locati	Chart review from Memorial hospitals in Miami	19/44% ESA in OR, 3 immediate deaths; pateints with ESA in OR had better survival	small study size (esp fro A	Could be b/c pts were in OR, or stable enough to transport to OR first?
Jaiganesh et al.	2012		QI project (?)	34	0	Survey sent to the health Trusts	Survey Answers	50 % had AE Ci-INH use guidelines; 55% had the med avail in the ED	Not a true study, since didn't address whether guidelines useful/successful	Only looked at ED with immunodeficiency depts attached. Better would be to look at all ED in the UK/geographical area…

Appendix D (Cont.)

Study	Year	LOE	Type of Study	Sample Size	Control Group	Method of testing	Source of Data	Findings	Weaknesses	Considerations
Jaiganesh	2013	7	expert opinion			"expert opinion and findings of literature searches" PubMed	ED and immunologist MD panel	Developed algorithm for AE form determinance and tx methods	expert opinion No study completed	Follow up to 2012 article. Guideline further refined
Bernstein et al	2015	2	triple blind RCT phase 2	26	24	meeting discharge criteria within 4hrs		31% ecallantide met d/c criteria vs 21% in placebo	only 10% increase. They are claiming signficant; does not address the severity of symptoms	
Lewis et al	2014	2	double blind phase 2 rct	20-10mg 19-30mg 20-60mg	18	meeting discharge criteria within 6hrs		no statistically sign difference btwn control and ecallantide BUT 100% v 60% in severe cases	although graded pts based on AE severity, this did not include a laryngeal assessment; they think maybe too many ppl who had less sever cases, so more likely to resove on its own anyway	study was stopped early as no signficance noted
Greve et	2016	4	retrospective case control	10	47	time to symptom resolution; intubation needs	chart review	pts received 1000IU of C1-INH; no intubations, signficantly shorter time to resolution (10hrs vs 33hrs) as determined by ENT MD	not a very large n#;	only looks at ACEi BK
Zuraw et	2010		Double blind RCT	35	33	Evaluation of pts based on list of symptoms	Data collection by ED and ENT MD	Statistically shorter time to symptom relief and symptom resolution	Time to complete resolution may be skewed for control group, as all participants who did not have symptom relief at 4 hrs recevied C1-INH	Only looks at HAE, which lots already said this tx works for

Appendix E

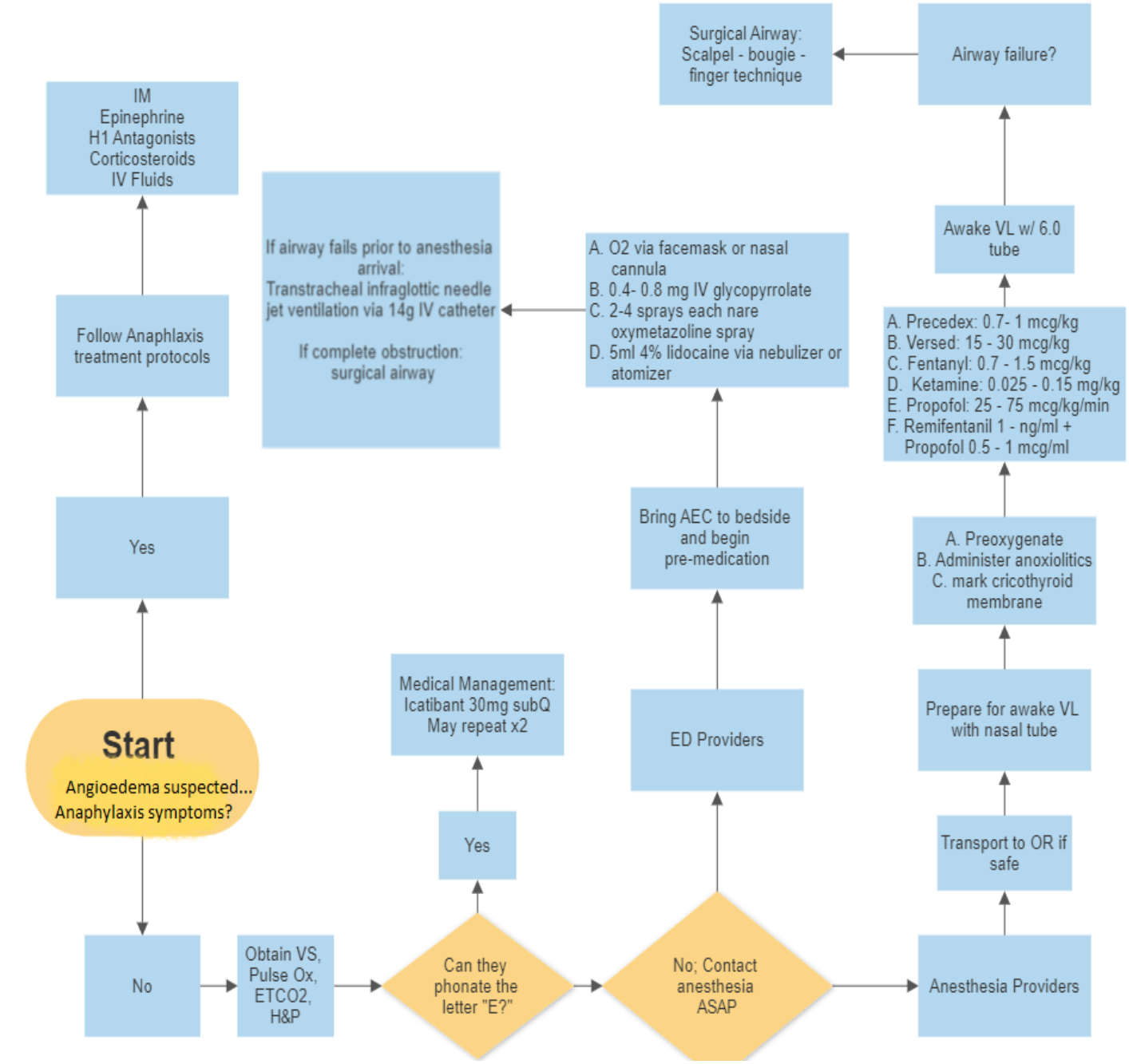
Scalpel – Finger – Bougie Technique



Reproduced from - Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. C. Frerk, V. S. Mitchell, A. F. McNarry, C. Mendonca, R. Bhagrath, A. Patel, E. P. O'Sullivan, N. M. Woodall and I. Ahmad, Difficult Airway Society intubation guidelines working group. *British Journal of Anaesthesia*, 115 (6): 827–848 (2015) doi:10.1093/bja/aev371

Appendix F

Angioedema Guideline Algorithm



Appendix G

Evidence Based Practice Angioedema Guideline Staff Handout

ED Provider Tasks

1. Do symptoms present as anaphylaxis?
    a. Yes: treat with anaphylaxis protocols (Epinephrine, H1 antagonists, corticosteroids, intravenous fluids).
    b. No: Continue with guideline.
2. Non anesthesia provider identifies case as angioedema.
    a. Vital signs on admit: ETCO2 monitoring is more beneficial than pulse Ox, but ETCO2 can still be "normal" until too late.
    b. H&P: Look for lip/facial swelling, GI symptoms, history/family history or angioedema, current medications, recent trauma (HAE), speed of onset (histamine AE usually faster onset than bradykinin induced), home premedication/treatment attempts, itching.
    c. Presence of stridor, hoarseness, voice changes, etc.

    "The patient should be asked to phonate "E" with a high pitch, as a patient able to complete this maneuver is unlikely to have laryngeal edema" (Long et al., 2019, p. 590).

        1) Patient can phonate "E," medication management only.
        2) Administer Icatibant: 30mg subcutaneously, may repeat x2.
3. If patient cannot phonate "E," contact anesthesia ASAP!
4. DO NOT MANIPULATE AIRWAY! (Even for a "look").
5. Get angioedema airway cart.

Appendix G (Cont.)

6. **While waiting for anesthesia**
    a. Avoid airway manipulation.
    b. Begin O2 delivery via facemask or nasal cannula.
        a. No nasal trumpet or positive pressure ventilation.
    c. Administer premedication.
        a. Glycopyrrolate 0.4-0.8mg IVP.
        b. Oxymetazoline spray: 2-4 sprays per nostril.
        c. Lidocaine 4%: 5ml via atomizer or nebulizer.
        d. Icatibant: 30mg subcutaneously, may repeat x 2.
        e. Judicious use of anxiolytic medications (patient MUST maintain own airway!)

If airway fails prior to anesthesia arrival:

7. Is the airway COMPLETELY obstructed?
    a. No: Needle cricothyrotomy/infraglottic transtracheal jet vent ventilation.
        i. Insert 14g IV needle in the cricothyroid membrane.
        ii. Retains first pass airway attempt for anesthesia.
        iii. May open glottis and improve airway structure identification.
        iv. Do NOT use if airway is completely obstructed.
    b. Yes: Emergent Surgical Airway.
8. No laryngeal mask airways! – does not go past area of airway stricture.

Appendix G (Cont.)

Anesthesia Tasks

9. Transport patient to the operating room if time and patient condition allow!
    a. Allows for greater familiarity with equipment.
    b. Increased airway experienced staff availability.
10. Premedicate for awake nasal intubation with video laryngoscopy.
    a. Preoxygenate/denitrogenate.
    b. Administer nebulized/atomized lidocaine, intranasal oxymetazoline, and IV glycopyrrolate if not done in ED.
    c. Titration of sedation medications selected based on patient presentation.

    PATIENT MUST MAINTAIN OWN AIRWAY!!

        i. Dexmedetomidine: 0.7-1mcg/kg bolus; 0.5-1mcg/kg/hr infusion
        ii. Midazolam: 15-30 mcg/kg
        iii. Fentanyl: 0.7-1.5 mcg/kg
        iv. Ketamine: 0.025-0.15 mg/kg
        v. Propofol: 25-75 mcg/kg/min
        vi. Remifentanil 1-3ng/ml + Propofol 0.5-1mcg/ml combo (do not use remifentanil alone)
        vii. Avoid NMBD!

    Ketamine MAY be the best choice, as it best maintains patient airway reflexes.
11. Mark cricothyroid membrane with skin marker prior to attempting any interventions.

Appendix G (Cont.)

12. Ensure all emergency surgical airway equipment OPEN and in reach at the patient bedside.
13. Perform awake intubation.
    a. Increased chance of airway success with nasal tracheal placement.
        i. AE is less likely to present with nasopharyngeal involvement.
    b. Use provided video laryngoscope in AEC for airway placement.
    c. Use smaller diameter tube (6.0) to allow for easier passage.
    d. If unable to pass NTT or visualize glottic opening, QUICKLY defer to surgical airway.
14. Surgical Airway
    a. Surgical airway performed as scalpel- bougie technique learned in skills lab.
    b. Use no. 20 scalpel to cut horizontal incision into previously marked cricothyroid membrane (results in 1.5cm incision).
    c. Rotate scalpel 90 degrees, with blade pointing caudally.
    d. Insert gum elastic bougie (GEB) into incision.
    e. Pass 6.0 ETT over GEB into airway and remove GEB.
15. After Airway placed
    a. Inflate retention balloon.
    b. Ensure ETCO2 return on monitor; confirm bilateral breath sounds.
    c. Secure Airway.
    d. Sedate/paralyze patient as needed.

Appendix H

Angioedema Cart Supplies

AE Cart	$1,250
King Vision Video Laryngoscope w/ Disposable Blades	$,1540
Multiple sized ETT	$1.27 each
Gum Elastic Bougie	$28.25
Disposable Scalpel	$17.60
Epinephrine	$7.02
IV Dexamethasone	$5.57
Icatibant	$2,671.38
Etomidate	$41.50
Succinylcholine	$8.18
Rocuronium	$5.78
Neo synephrine-Afrin	$5.12
Glycopyrrolate	$40.26
Nebulized Lidocaine	$22.98
Additional supplies from Central Supply	Value obtained after definitive cart contents decided

(Global, 2022; Altsourcemedical, 2022; Ohio Health, 2022)

Note. Medication costs as designated Medicare/Medicaid contracted rates.

Appendix I

Creating a Patient List for Data Extraction Via ICD Code Designation

To create a patient list by ICD codes in Epic Care Connect, perform the following steps:

1. “From the main Epic button, navigate to Reports > My Reports > Library.
2. Search for Diagnosis in the search box at the top.
3. From the list produced, select My Patients with <X> Problem list Diagnosis report.
4. Select Edit.
5. Select Choose Criteria.
6. Search for and select Diagnosis by Code. Select Accept.
7. In the appropriate fields, enter appropriate diagnosis code and set.
8. Select Run to obtain a Patient List Report” (GSK plc, 2018, pp. 2-3).