VENTOR Study

Focus Group Discussion with Medical Care Providers

House Keeping Items

- Today’s meeting is being recorded
- All of today’s materials seen/provided today can be found at the studies website: www.ventorstudy.com

Today’s Agenda

- Current resuscitation guidelines and priorities during CPR
- Discuss the optimal ventilation strategy during CPR
- Introduction of the Ventor Airway System
- Review the VENTOR study design
- Key safety and effectiveness endpoints/observations
- Risk and Benefits analysis of the VENTOR study
- Exception From Informed Consent criteria
- Ways to give feedback.

Need for Improved Airway and Ventilation Alternatives in IHCA

- Nearly 290,000 hospitalized patients suffer from cardiac arrest annually in the U.S.
- Causes of medical arrest vary from:
  - Acute coronary syndrome (~50%)
  - Dysrhythmia (~20%)
  - Sepsis (~10%)
  - OD (~8%)
  - Respiratory failure (~5%)
  - Stroke (~5%)
- Survival rates for in-hospital cardiac arrest (IHCA) are less than 25% to discharge.
- Of which only half will survive neurologically intact

Purpose of CPR:

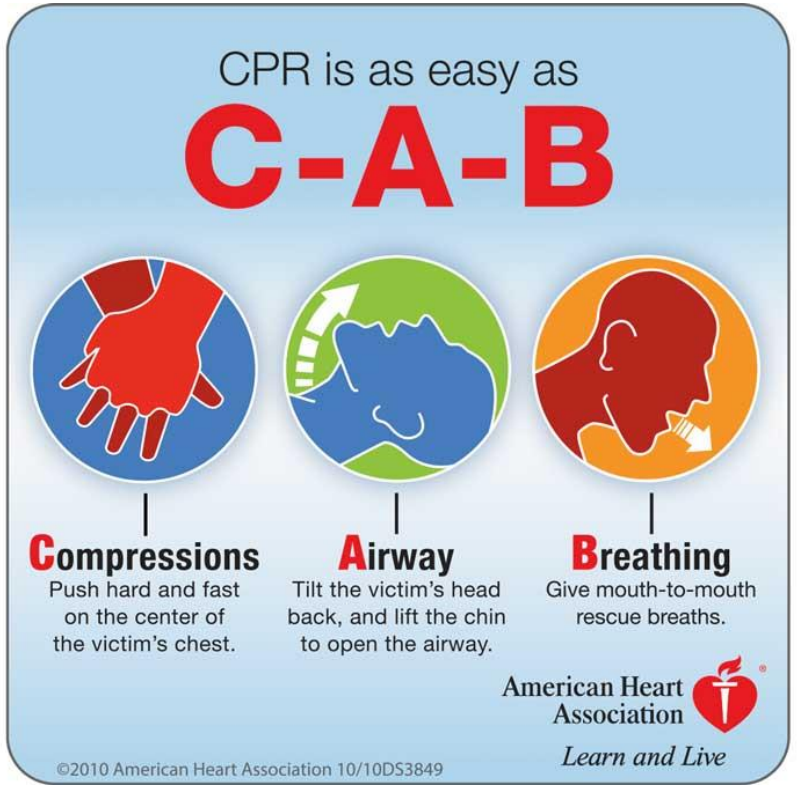
Sustain patient viability until underlying cause is addressed

By:

Ensuring circulation of oxygen and glucose until definitive treatment arrives/reached

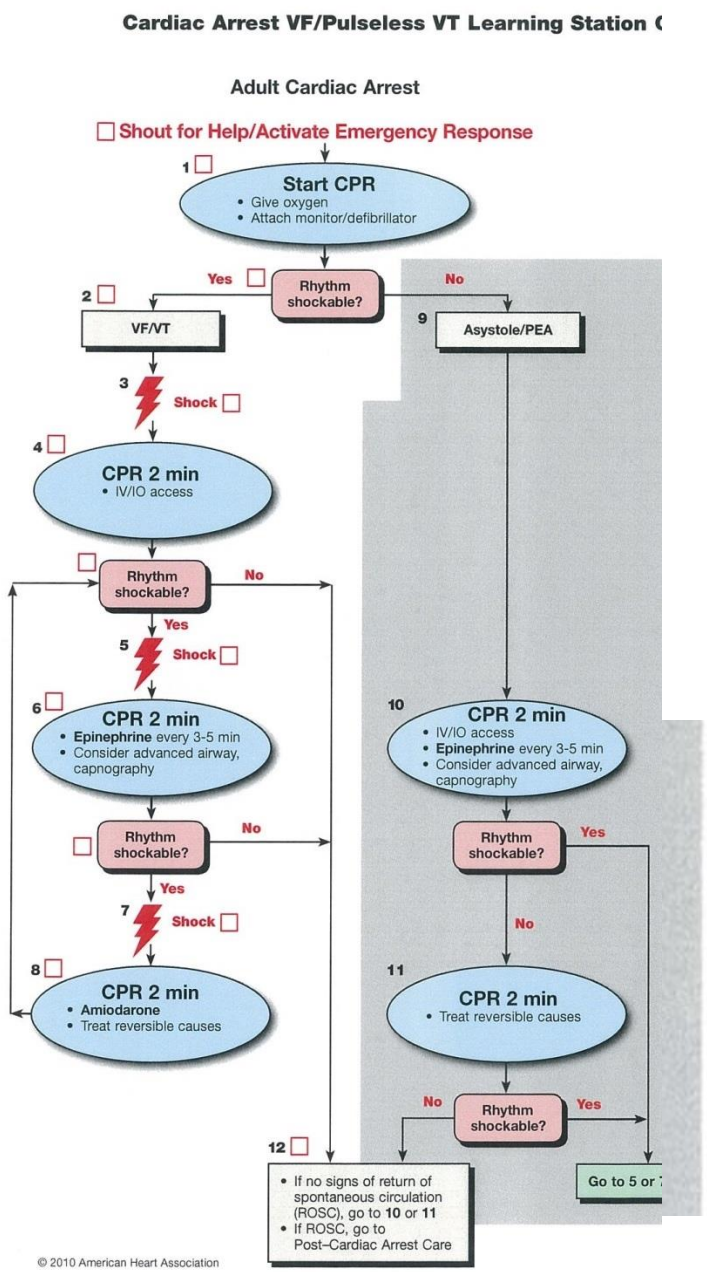
Priorities:

The American Heart Association has continued to emphasize compressions over ventilation



The AHA has even deemphasized airway management for ACLS care providers

- Without advanced airway chest compression to ventilation ration is 30:2
- Advanced Airway placement is the last ACLS intervention and its only “consider”



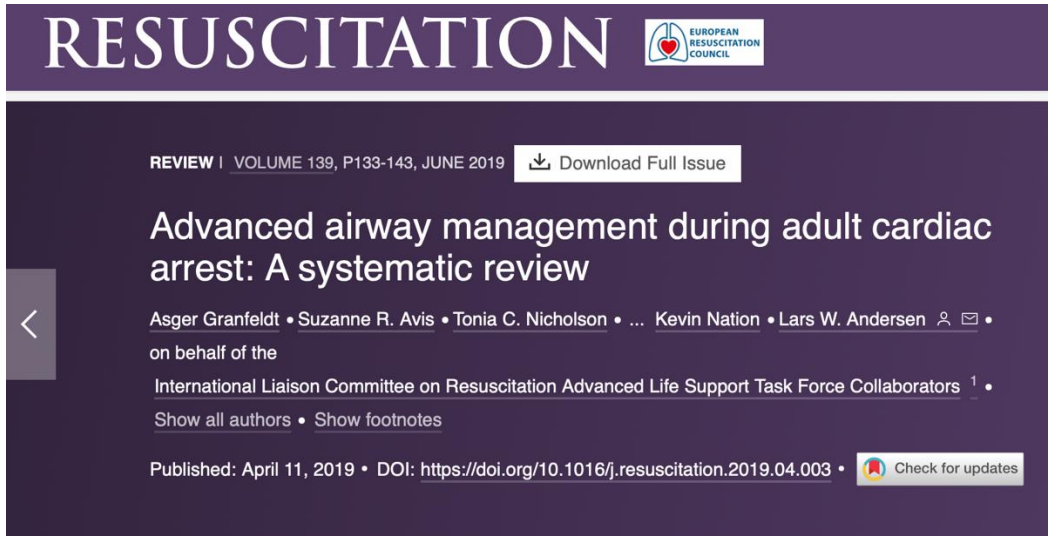
Advanced Airway

- Supraglottic advanced airway or endotracheal intubation
- Waveform capnography to confirm and monitor ET tube placement
- 8-10 breaths per minute with continuous chest compressions

Why does the AHA continue to deemphasize airway and ventilation?

Is it not important or just hard to do right?

What does research suggest:



Aim

To systematically review the literature on advanced airway management during adult cardiac arrest in order to inform the International Liaison Committee of Resuscitation (ILCOR) consensus on science and treatment recommendations.

Methods

The review was performed according to PRISMA guidelines and registered on PROSPERO (CRD42018115556). We searched Medline, Embase, and Evidence-Based Medicine Reviews for controlled trials and observational studies published before October 30, 2018. The population included adult patients with cardiac arrest. Two investigators reviewed studies for relevance, extracted data, and assessed the risk of bias of individual studies.

Results

We included 78 observational studies and 11 controlled trials. Most of the observational studies and all of the controlled trials only included patients with out-of-hospital cardiac arrest. The risk of bias for individual observational studies was overall assessed as critical or serious, with confounding and selection bias being the primary sources of bias. Three of the controlled trials, all published in 2018, were powered for clinical outcomes with two comparing a supraglottic airway to tracheal intubation and one comparing bag-mask ventilation to tracheal intubation. All three trials had some concerns regarding risk of bias primarily due to lack of blinding and variable adherence to the protocol. Clinical and methodological heterogeneity across studies, for both the observational studies and the controlled trials, precluded any meaningful meta-analyses.

Conclusions

We identified a large number of studies related to advanced airway management in adult cardiac arrest. Three recently published, large randomized trials in out-of-hospital cardiac arrest will help to inform future guidelines. Trials of advanced airway management during in-hospital cardiac arrest are lacking.

Circulation

ORIGINAL RESEARCH ARTICLE

Bag-Valve-Mask Ventilation and Survival From Out-of-Hospital Cardiac Arrest: A Multicenter Study

Ahamed H. Idris, MD; Elisabete Aramendi Ecenarro, PhD; Brian Leroux, PhD; Xabier Jaureguibeitia, MSc; Betty Y. Yang, MD, MS; Sarah Shaver, MD; Mary P. Chang, MD, MPH; Tom Rea, MD, MPH; Peter Kudenchuk, MD; Jim Christenson, MD; Christian Vaillancourt, MD, MSc; Clifton Callaway, MD, PhD; David Salcido, PhD; Jonas Carson; Jennifer Blackwood, MPH; Henry E. Wang, MD, MS, MPH

BACKGROUND: Few studies have measured ventilation during early cardiopulmonary resuscitation (CPR) before advanced airway placement. Resuscitation guidelines recommend pauses after every 30 chest compressions to deliver ventilations. The effectiveness of bag-valve-mask ventilation delivered during the pause in chest compressions is unknown. We sought to determine: (1) the incidence of lung inflation with bag-valve-mask ventilation during 30:2 CPR; and (2) the association of ventilation with outcomes after out-of-hospital cardiac arrest.

METHODS: We studied patients with out-of-hospital cardiac arrest from 6 sites of the Resuscitation Outcomes Consortium CCC study (Trial of Continuous Compressions versus Standard CPR in Patients with Out-of-Hospital Cardiac Arrest). We analyzed patients assigned to the 30:2 CPR arm with ≥2 minutes of thoracic bioimpedance signal recorded with a cardiac defibrillator/monitor. Detectable ventilation waveforms were defined as having a bioimpedance amplitude ≥0.5 Ω (corresponding to ≥250 mL V_T) and a duration ≥1 s. We defined a chest compression pause as a 3- to 15-s break in chest compressions. We compared the incidence of ventilation and outcomes in 2 groups: patients with ventilation waveforms in <50% of pauses (group 1) versus those with waveforms in ≥50% of pauses (group 2).

RESULTS: Among 1976 patients, the mean age was 65 years; 66% were male. From the start of chest compressions until advanced airway placement, mean±SD duration of 30:2 CPR was 9.8±4.9 minutes. During this period, we identified 26861 pauses in chest compressions; 60% of patients had ventilation waveforms in <50% of pauses (group 1, n=1177), and 40% had waveforms in ≥50% of pauses (group 2, n=799). Group 1 had a median of 12 pauses and 2 ventilations per patient versus group 2, which had 12 pauses and 12 ventilations per patient. Group 2 had higher rates of prehospital return of spontaneous circulation (40.7% versus 25.2%; $P<0.0001$), survival to hospital discharge (13.5% versus 4.1%; $P<0.0001$), and survival with favorable neurological outcome (10.6% versus 2.4%; $P<0.0001$). These associations persisted after adjustment for confounders.

CONCLUSIONS: In this study, lung inflation occurred infrequently with bag-valve-mask ventilation during 30:2 CPR. Lung inflation in ≥50% of pauses was associated with improved return of spontaneous circulation, survival, and survival with favorable neurological outcome.

Profession BVM Ventilations: Essential for patient outcomes but inadequately performed in most cases

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SAGE

Association of Arterial Oxygen Tension During In-Hospital Cardiac Arrest With Return of Spontaneous Circulation and Survival

Jignesh K. Patel, MD[1], Elinor Schoenfeld, PhD[2], Puja B. Parikh, MD, MPH[3], and Sam Parnia, MD, PhD[1]

Background

•IHCA remains linked to high morbidity and mortality despite advances.

•Study goal: Assess impact of arterial oxygen tension (PaO2) on ROSC and survival to discharge in IHCA patients.

Methods

•255 IHCA patients, January 2012 - December 2013.

•167 had arterial blood gas tested during arrest.

•Primary outcome: Survival to discharge; Secondary: ROSC.

Results

•Higher PaO2 linked to conditions like hypertension, CKD.

•Consistent IHCA presentation across PaO2 groups.

•Higher PaO2 showed increased ROSC rates (58%-100%) and survival (16%-56%).

Conclusion

•Higher intra-arrest PaO2 independently linked to better survival outcomes in IHCA.

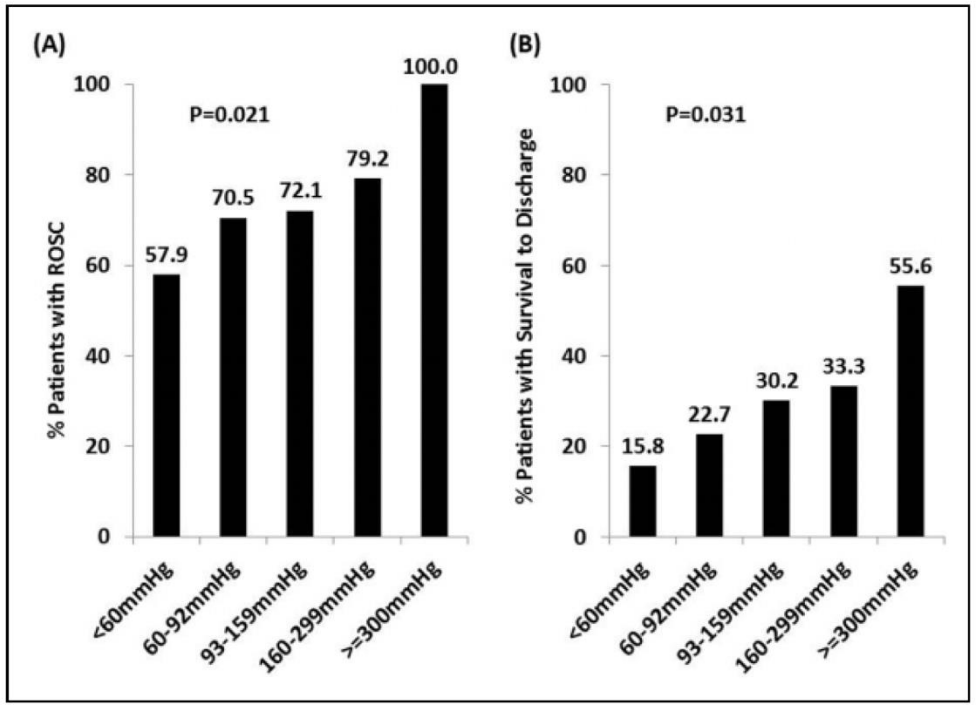


Figure 2. Rates of (A) return of spontaneous circulation (ROSC) and (B) survival to hospital discharge according to Pa_{O_2} group in adults with in-hospital cardiac arrest.

Table 4. Multivariate Analysis of Predictors of Survival to Discharge.[a]

	Odds Ratio	95% CI	*P* Value
Pa_{O_2} < 60 mm Hg (referent)	-	-	-
60 mm Hg ≤ Pa_{O_2} < 93 mm Hg	3.95	0.44-35.40	.220
93 mm Hg ≤ Pa_{O_2} < 160 mm Hg	6.79	0.83-55.76	.075
160 mm Hg ≤ Pa_{O_2} < 300 mm Hg	8.70	0.63-120.26	.106
Pa_{O_2} ≥ 300 mm Hg	60.68	3.04-1210.28	.007

Abbreviation: CI, confidence interval.

[a]Variables included in the model: Pa_{O_2} group, age, initial rhythm, chronic obstructive pulmonary disease, serum potassium, arterial pH, arterial P_{CO_2}, and serum blood urea nitrogen.

Higher oxygenation (PaO2) is correlated with improved survival.

Unclear if PaO2 variation is due to patient condition, CPR quality, or ventilation effectiveness.

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Tracheal Intubation During Adult In-Hospital Cardiac Arrest and Survival

Lars W. Andersen, MD, MPH, PhD; Asger Granfeldt, MD, PhD, DMSc; Clifton W. Callaway, MD, PhD; Steven M. Bradley, MD, MPH; Jasmeet Soar, FRCA, FFICM, FRCP; Jerry P. Nolan, FRCA, FRCP, FFICM, FCEM (Hon); Tobias Kurth, MD, ScD; Michael W. Donnino, for the American Heart Association's Get With The Guidelines–Resuscitation Investigators

IMPORTANCE Tracheal intubation is common during adult in-hospital cardiac arrest, but little is known about the association between tracheal intubation and survival in this setting.

OBJECTIVE To determine whether tracheal intubation during adult in-hospital cardiac arrest is associated with survival to hospital discharge.

DESIGN, SETTING, AND PARTICIPANTS Observational cohort study of adult patients who had an in-hospital cardiac arrest from January 2000 through December 2014 included in the Get With The Guidelines–Resuscitation registry, a US-based multicenter registry of in-hospital cardiac arrest. Patients who had an invasive airway in place at the time of cardiac arrest were excluded. Patients intubated at any given minute (from 0-15 minutes) were matched with patients at risk of being intubated within the same minute (ie, still receiving resuscitation) based on a time-dependent propensity score calculated from multiple patient, event, and hospital characteristics.

EXPOSURE Tracheal intubation during cardiac arrest.

MAIN OUTCOMES AND MEASURES The primary outcome was survival to hospital discharge. Secondary outcomes included return of spontaneous circulation (ROSC) and a good functional outcome. A cerebral performance category score of 1 (mild or no neurological deficit) or 2 (moderate cerebral disability) was considered a good functional outcome.

RESULTS The propensity-matched cohort was selected from 108 079 adult patients at 668 hospitals. The median age was 69 years (interquartile range, 58-79 years), 45 073 patients (42%) were female, and 24 256 patients (22.4%) survived to hospital discharge. Of 71 615 patients (66.3%) who were intubated within the first 15 minutes, 43 314 (60.5%) were matched to a patient not intubated in the same minute. Survival was lower among patients who were intubated compared with those not intubated: 7052 of 43 314 (16.3%) vs 8407 of 43 314 (19.4%), respectively (risk ratio [RR] = 0.84; 95% CI, 0.81-0.87; $P < .001$). The proportion of patients with ROSC was lower among intubated patients than those not intubated: 25 022 of 43 311 (57.8%) vs 25 685 of 43 310 (59.3%), respectively (RR = 0.97; 95% CI, 0.96-0.99; $P < .001$). Good functional outcome was also lower among intubated patients than those not intubated: 4439 of 41 868 (10.6%) vs 5672 of 41 733 (13.6%), respectively (RR = 0.78; 95% CI, 0.75-0.81; $P < .001$). Although differences existed in prespecified subgroup analyses, intubation was not associated with improved outcomes in any subgroup.

CONCLUSIONS AND RELEVANCE Among adult patients with in-hospital cardiac arrest, initiation of tracheal intubation within any given minute during the first 15 minutes of resuscitation, compared with no intubation during that minute, was associated with decreased survival to hospital discharge. Although the study design does not eliminate the potential for confounding by indication, these findings do not support early tracheal intubation for adult in-hospital cardiac arrest.

Importance

- Tracheal intubation is common in adult IHCA, but its impact on survival is unclear.

Objective

- Assess whether tracheal intubation during IHCA affects survival to discharge.

Design & Participants

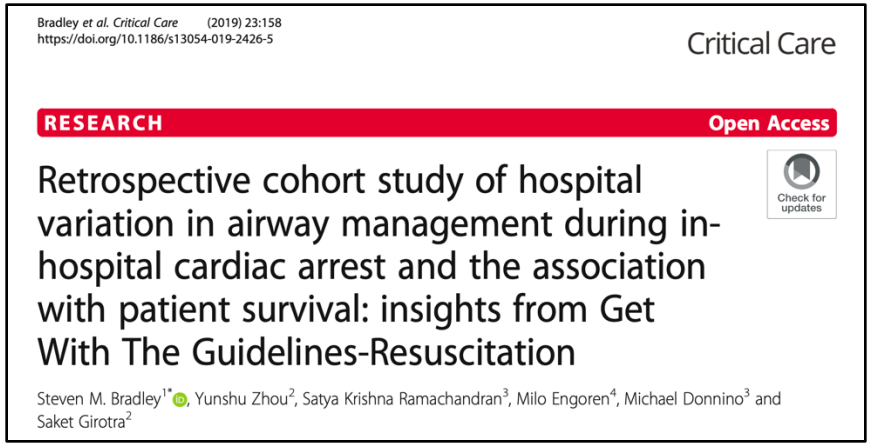
- Observational cohort of adults in IHCA (2000-2014) from the *Get With The Guidelines–Resuscitation* registry.
- Excluded patients with pre-existing invasive airway.
- Matched intubated and non-intubated patients using time-dependent propensity scores.

Results

- 108,079 patients; median age 69, 42% female, 22.4% survived to discharge.
- Survival lower in intubated patients (16.3%) vs. non-intubated (19.4%) (RR = 0.84, P < .001).
- ROSC lower in intubated (57.8%) vs. non-intubated (59.3%) (RR = 0.97, P < .001).
- Good functional outcome lower in intubated (10.6%) vs. non-intubated (13.6%) (RR = 0.78, P < .001).
- No subgroups showed improved outcomes with intubation.

Conclusions

- Early tracheal intubation in IHCA linked to decreased survival.
- Findings do not support early intubation in adult IHCA.


Bradley et al. Critical Care (2019) 23:158
https://doi.org/10.1186/s13054-019-2426-5

Critical Care

RESEARCH Open Access

Retrospective cohort study of hospital variation in airway management during in-hospital cardiac arrest and the association with patient survival: insights from Get With The Guidelines-Resuscitation

Steven M. Bradley[1*], Yunshu Zhou[2], Satya Krishna Ramachandran[3], Milo Engoren[4], Michael Donnino[3] and Saket Girotra[2]

Importance

The best approach to airway management during IHCA is still unknown.

Objective

Analyze hospital-level variations in endotracheal intubation during CPR for IHCA and its impact on survival.

Design, Setting, Participants

- Retrospective cohort study (2000-2016) at *Get With The Guidelines-Resuscitation* hospitals.
- Hospitals categorized into quartiles based on intubation rates during CPR.
- Risk-adjusted models assessed the link between intubation rates and survival.

Results

- 155,252 IHCA patients across 656 hospitals; 69.7% received intubation, with 24.8% survival to discharge.
- Inverse association between hospital intubation rate and survival (highest vs. lowest quartile, OR = 0.81; 95% CI, 0.74-0.90; P < .001).
- Association impacted by pre-arrest respiratory failure, with lower survival in high-intubation hospitals only in patients without prior respiratory failure.

Conclusion

- Intubation rates during CPR vary widely across hospitals and are inversely linked to survival in IHCA, especially in patients without prior respiratory failure.
- Identifying optimal airway management strategies may improve IHCA outcomes.

The Ventor Airway System

- A new investigational airway and ventilation device designed to improve oxygen delivery during CPR.
- Easy to insert and designed to synchronize with chest compressions.
- Aims to enhance the effectiveness of resuscitation efforts and improve patient outcomes.
- Potential to reduce complications associated with traditional airway management techniques.

VENTOR Device Demo and Discussion

VENTOR Study Design

- Inclusion Criteria
- Exclusion Criteria
- Study Conduct
- Safety Observations
- Effectiveness Observations
- Study Schema

Inclusion Criteria

- Adults aged 18-75 years, inclusive
- IHCA (non-traumatic)
- At least 4 feet in height

Exclusion Criteria

1. Intubated with an endotracheal tube
2. Valid DNAR or study opt-out bracelet (including previous enrollment bracelet)
3. LAR or Family member objects to enrollment
4. Obvious signs of irreversible death (rigor mortis, dependent lividity, decapitation, transection, decomposition)
5. Responsive with an intact gag reflex
6. Blunt, penetrating, or burn-related injury, drowning, or electrocution
7. Known upper airway foreign body or mass
8. Lower airway obstruction
9. Dental gap of < 2 cm
10. Ingested caustic substances
11. Medicine Admitting Note's medical history is incomplete or has only been completed by an emergency physician.

Exclusion Criteria (continued)

12. Known esophageal disease or facial/perforating neck trauma defined as study candidates with the following medical history:

a. Diseases:

a) Esophageal Varices

b) Esophageal Cancer

c) Esophageal Strictures

b. Any patient on the following medications will be excluded:

Oxaliplatin, Leucovorin, Fluorouracil

c. Any patient with the following examination findings will be excluded:

Caput medusae, History or evidence of vomiting blood

13. Known vulnerable subject (e.g.: prisoner, pregnancy, terminal illness, dementia, with the exception of Inclusion #2)

14. History of medical, surgical, or other conditions that, in the opinion of the investigator, would limit study participation

Study Conduct

- **Enrollment**
- Up to 25 IHCA subjects, enrolled in 5-subject increments
- Enrollment by operator after eligibility confirmation
- **Procedure**
- Initial supraglottic airway (non-ET) removed by study personnel
- Ventor Airway System used exclusively by certified and trained professionals
- **Standard of Care**
- All other resuscitation follows ACLS guidelines (compressions, defibrillation, drugs)
- **Study Measures**
- Focus: Initial safety and effectiveness of Ventor Airway System
- Assessed on ventilation and oxygenation performance during CPR
- **Study Timeline**
- Participation from Ventor Airway use through hospital course
- Ends at 3-month follow-up or upon death

Study Monitoring

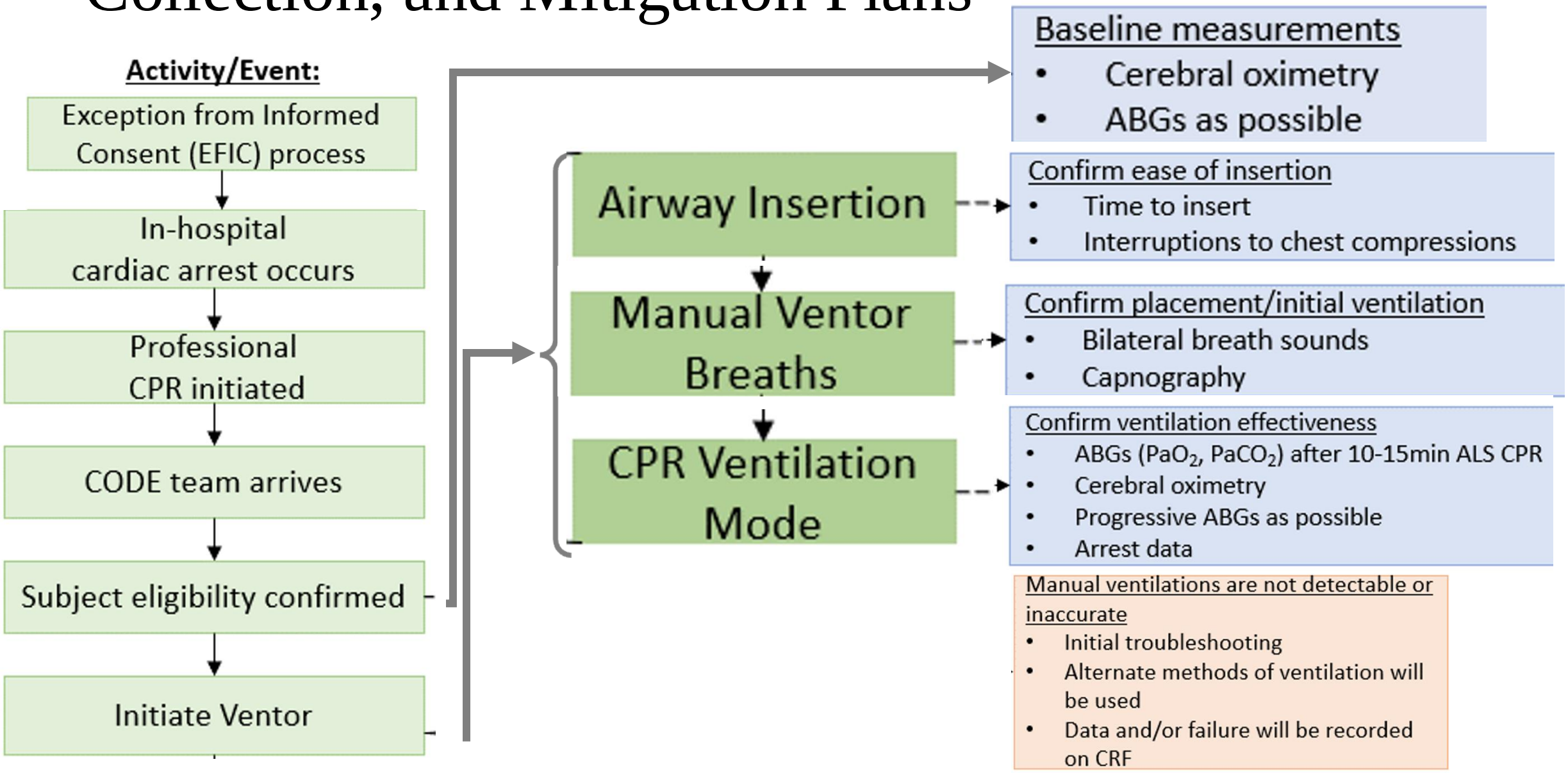
Clinical Events Committee (CEC)

Data and Safety Monitoring Board (DSMB)

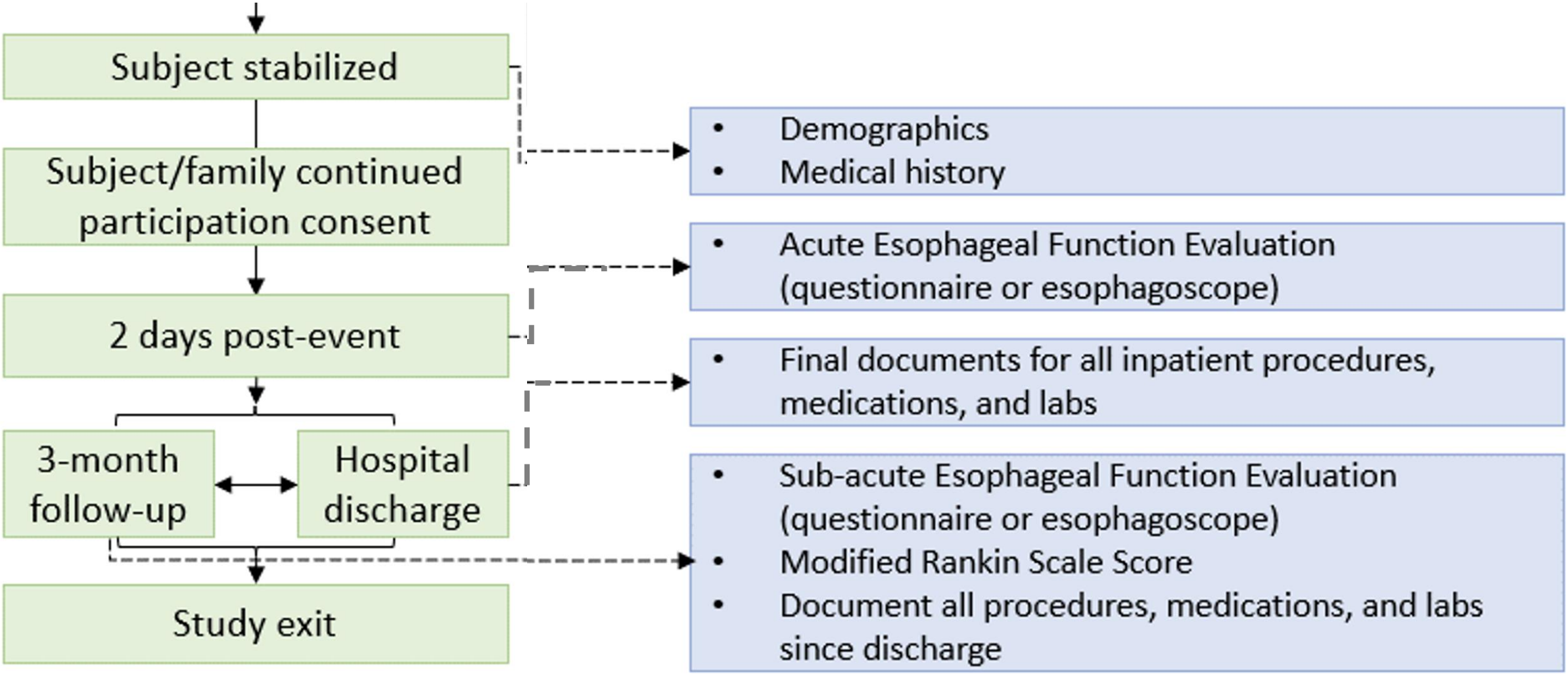
Stony Brook Institutional Review Board (IRB)

Staged Reporting to FDA

Study Schema – Device Use Activity, Data Collection, and Mitigation Plans



Study Schema – Post-treatment Activity and Data Collection



Safety Observations

SAE Analysis: Assess type, frequency, and device/procedure relationship for all SAEs. Unrelated SAEs assessed separately.

- **Esophageal-Related**: Track any esophageal trauma or GI issues linked to the Ventor Airway System (per CEC adjudication) at:
  - Initial device use
  - 2-day evaluation (questionnaire or esophagoscopic)
  - 3-month evaluation (questionnaire or esophagoscopic)
  - Any time during enrollment
- **Asphyxia-Related**: Analyze any asphyxia physiology attributed to the Ventor Airway System (per CEC adjudication).

Effectiveness Observations

Ease of airway insertion

- Number of attempts
- Duration of insertion process
- Duration of interruptions to chest compressions

Patency of Ventor Airway

- Accuracy of location identification and monitoring
- Ability to properly pressurize lungs
- Incidences of regurgitation and/or aspiration

CPR mode ventilation effect on:

- Intra-arrest ABG (including but not limited to PaO2 and PaCO2)
- Cerebral oximetry
- $EtCO_2$

Effect of the Ventor Airway System on:

- ROSC rate
- Time of unassisted breathing
- Survival rate to 2 days, discharge (if before 3 month evaluation), and 3 months.

Neurological assessment: mRS score at 2 days and at 3 months post-event

What to do if CODE team responds to my department?

- Discuss in which departments the CODE and VENTOR study will be conducted
- Discuss how to support the study
- Discuss how to educate other care providers on the possibilities of the VENTOR study

Risk Associated with the VENTOR Study

- Device-Specific Risks
- Operational Risks
- Study-Related Risks
- General Clinical Research Risks

Device-Specific Risks

- **Airway Misidentification**: Potential for incorrect determination of trachea or esophagus, reducing ventilation effectiveness. Despite extensive pre-clinical testing, continuous monitoring and alarms are necessary to mitigate this risk.
- **Esophageal Trauma**: The use of negative pressure to seal the esophagus could cause tissue trauma, particularly in patients with pre-existing esophageal conditions. This is mitigated by excluding patients with known esophageal disease and limiting device use to <1 hour.
- **Ventilation Issues**: Potential for hypoventilation or hyperventilation, particularly in real-world emergency settings. The device's automated synchronization with chest compressions aims to reduce these risks.
- **Mechanical Failures**: Issues like incorrect ventilation rates, battery failure, or environmental damage. Mitigated by having alternative ventilation equipment available and detailed proctoring.
- **User-Related Issues**: Improper setup or operation of the device, skill decay, and potential transport difficulties. Comprehensive training and user manuals aim to address these issues.
- **Unknown Risk:** There is always the concern of unknown risk when studying a novel device

Operational Risks

- **Difficulty in Airway Insertion**: Insertion challenges leading to delays in establishing an airway. The device's design aims to reduce these difficulties, supported by comprehensive user training and limitations on insertion attempts.
- **Aspiration and Infection**: High likelihood of aspiration due to reduced gag reflex and increased gastric distension during CPR. The Ventor includes suction capabilities, but limitations exist for subglottic suctioning when placed in the esophagus.
- **Improper Ventilation Pressures**: Risks of barotrauma and gas trapping. The device includes pressure-sensing alarms and mechanical relief valves to mitigate these risks.

Study-Related Risks

- **Additional Procedures**: Risks associated with intra-arrest ABG sampling and cerebral oximetry monitoring, including delayed care and potential inaccuracies in readings. Proper timing and training are crucial to minimize these risks.
- **Esophagoscopy Risks**: Post-event esophagoscopy introduces sedation risks, mitigated by performing the procedure only on unresponsive or already-sedated patients.

General Clinical Research Risks

- **Improper Subject Consenting**: Challenges with EFIC processes and ensuring comprehensive community consultation and subject/family notification.
- **Enrolling Ineligible Subjects**: Risks of including patients with contraindicated conditions, such as esophageal disease, and ensuring operator awareness of device limitations through rigorous training.
- **Study Execution Issues**: Risks of data collection failures, slow enrollment, and confidentiality breaches. Controlled in-hospital settings, strong support from the sponsor, and experienced PI selection help mitigate these risks.

Potential VENTOR Benefits

- Enhanced Oxygenation and Survival
- Ease of Use and Rapid Airway Management
- Consistent and Automated Ventilation
- Contribution to Medical Knowledge

Enhanced Oxygenation and Survival

- **Improved PaO2 Levels**: Demonstrated superior outcomes in animal studies, with higher intra-arrest arterial partial pressure of oxygen (PaO2) and more balanced partial pressure of CO2 (PaCO2) levels, correlating with increased survival rates and better neurological outcomes.
- **Return of Spontaneous Circulation (ROSC)**: Higher rates of ROSC observed in pre-clinical studies, indicating effective ventilation and perfusion.

Ease of Use and Rapid Airway Management

- **Simplified Insertion**: Easier and quicker to insert compared to traditional endotracheal intubation, with users showing higher ease-of-use ratings and faster insertion times in comparative cadaver studies.
- **Blind Insertion Capability**: Designed for blind insertion, reducing the need for visualization tools and skills, making it suitable for use in high-stress, emergency situations.

Consistent and Automated Ventilation

- **Synchronized Ventilation**: Automates and synchronizes ventilation with chest compressions, ensuring consistent and effective delivery of breaths, which is crucial during CPR.
- **Reduced User Error**: Automation reduces the risk of hypo- or hyperventilation, common in manual ventilation methods, particularly in chaotic emergency settings.

Contribution to Medical Knowledge

- **Early Feasibility Study Data**: Provides valuable data on the initial safety and effectiveness of the device, contributing to the broader understanding of airway management and resuscitation techniques.
- **Addressing Unmet Needs**: Addresses critical gaps in current resuscitation practices, offering potential improvements in patient care and outcomes during cardiac arrest.

How are emergency studies different?

- Specific Federal regulations allow for exception from informed consent for emergency research or EFIC
- EFIC is only allowed when:
  - The condition under study is life threatening
  - Existing treatment are unproven or inadequate
  - There is potential benefit for patients
  - Informed consent cannot be obtained.

What do you think about VENTOR?

- The study hasn’t started yet, so we want to hear your thoughts.
- Tell us about your experiences.
- Do you think it is OK for the study to be done?
- The study team and medical review board will consider your input in deciding whether it is OK for this study to be done in your community.

Requirements for EFIC

- Community consultation (why we are here)
- Public disclosure before and after study
- Oversight during study

How does EFIC work for VENTOR?

- If family member or representative is available during the screen of subject availability (approximately 3 minutes) they will decide for patient.
- If they are not available, eligible patients will be started in study without consent.
- Patients, family members, and representatives are told about the study as soon as possible and asked if they want the patient (or themselves) to continue in the study.

Can the anyone chose to opt-out of the study before a cardiac arrest event?

- Visit our website to print an Opt-Out Card.
- Contact our study team to request an Opt-Out Card, bracelet, or necklace.
- Carry the Opt-Out Card, bracelet, or necklace with you at all times during the study enrollment period.
- Inform your family and caregivers about your decision to opt-out of the study.
- In the event of a cardiac arrest, emergency medical personnel and hospital staff will look for the Opt-Out Card, bracelet, or necklace to respect your decision.

Questions?

- If you have any concerns or questions, please call us or contact us.
- Principal Investigator: [Name, phone number, email]
- Study Coordinator: [Name, phone number, email]