Published in final edited form as:

Resuscitation. 2016 April ; 101: 57–64. doi:10.1016/j.resuscitation.2016.01.012.

Design and Implementation of the Resuscitation Outcomes Consortium Pragmatic Airway Resuscitation Trial (PART)

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AUTHORS CONTRIBUTIONS

HEW, DKP, GN, HH and SWS designed the trial. HEW and GN obtained funding for the trial. HEW drafted the manuscript and all authors contributed to its critical review. HEW assumes overall responsibility for the paper.

CONFLICT OF INTEREST STATEMENT

The authors declare no financial or other conflicts of interest.

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Abstract

Airway management is an important component of resuscitation from out-of-hospital cardiac arrest (OHCA). The optimal approach to advanced airway management is unknown. The Pragmatic Airway Resuscitation Trial (PART) will compare the effectiveness of endotracheal intubation (ETI) and Laryngeal Tube (LT) insertion upon 72-hour survival in adult OHCA. Encompassing United States Emergency Medical Services agencies affiliated with the Resuscitation Outcomes Consortium (ROC), PART will use a cluster-crossover randomized design. Participating subjects will include adult, non-traumatic OHCA requiring bag-valve-mask ventilation. Trial interventions will include 1) initial airway management with ETI and 2) initial airway management with LT. The primary and secondary trial outcomes are 72-hour survival and return of spontaneous circulation. Additional clinical outcomes will include airway management process and adverse events. The trial will enroll a total of 3,000 subjects. Results of PART may guide the selection of advanced airway management strategies in OHCA.

Keywords

Intubation (Intratracheal); cardiopulmonary arrest; paramedic; emergency medical services; airway management; resuscitation; clinical trials

INTRODUCTION

Out-of-hospital cardiopulmonary arrest (OHCA) is a major public health problem affecting almost 400,000 adults in the United States each year, with less than 10% surviving.^{1,2} To optimize delivery of oxygen during cardiac arrest resuscitation, clinicians may perform endotracheal intubation (ETI). ETI provides a direct conduit to the lungs, facilitating easier and more controlled oxygen delivery, and potentially protecting the lungs from aspiration of vomitus.

Paramedics in North America commonly perform ETI when resuscitating OHCA. Although a standard paramedic practice for over 30 years, many studies underscore the complexity and pitfalls of ETI, including unrecognized tube misplacement, multiple and failed ETI attempts, iatrogenic hyperventilation, and prolonged interruptions in cardiopulmonary resuscitation chest compressions.^{3–11} US paramedic ETI training and individual opportunity to perform the procedure are also limited.^{12,13}

An alternative to ETI is the supraglottic airway (SGA), including devices such as the Laryngeal Mask Airway (LMA – LMA North America, San Diego, California, United States), Combitube (Covidien, Inc, Mansfield, Massachusetts, United States), i-gel (Intersurgical, Workingham, Berkshire, United Kingdom) and Laryngeal Tube (LT – King Systems, Inc, Noblesville, Indiana, United States).^{14,15} Compared with ETI, clinicians and medical directors believe that SGAs entail easier insertion technique and lower skill acquisition and maintenance thresholds, while exhibiting similar ventilatory characteristics. However, the comparative effectiveness of SGA over ETI upon OHCA outcomes remains unclear, with some observational cohort studies suggesting similar or better functional and overall survival with ETI than SGA.^{16–22} There have been no randomized controlled clinical trials comparing ETI and SGA in adult OHCA.^{23,24}

In this paper we describe the rationale for and design of the Resuscitation Outcomes Consortium Pragmatic Airway Resuscitation Trial (PART), a multicenter pragmatic randomized clinical trial comparing the effectiveness of ETI and LT insertion upon outcomes after OHCA.

METHODS AND ANALYSIS

Trial Organization

PART will be carried out by EMS agencies affiliated with the Resuscitation Outcomes Consortium (ROC), a North American network dedicated to conducting clinical trials of OHCA and major trauma.²⁵ PART will be jointly coordinated by the Alabama Regional Coordinating Center of ROC (Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham, Alabama) and the ROC Data Coordinating Center (Clinical Trials Center, University of Washington, Seattle, Washington). (Figure 1) EMS agencies affiliated with five United States ROC Regional Coordinating Centers (Alabama, Dallas, Milwaukee, Pittsburgh and Portland) will carry out the study.

Funding- Impact on Clinical Design

PART is supported by a special grant (UH2-HL125163) from the National Heart, Lung and Blood Institute (NHLBI) supporting large-scale, low-cost pragmatic clinical trials.²⁶ This new funding mechanism introduced several requirements that influenced the design of the trial:

- **Focus on pragmatic trial design.** A pragmatic trial focuses on the evaluation of interventions in real-world contexts. Pragmatic trials emphasize clinically relevant outcomes, with less attention paid to secondary, explanatory or mechanistic endpoints.
- **Structured implementation timeline.** The award stipulated a year 1 planning phase, with initiation of trial enrollment (years 2–5) after satisfaction of initial milestones.
- **Defined funding.** The grant provided US\$350,000 for the year 1 planning phase, and US\$500,000 per year for the trial enrollment phase.
- **Limited to US elements.** The conditions of the grant limited scientific participation to US institutions and investigators.

Trial Registration

PART is registered with www.clinicaltrials.gov as trial no. NCT02419573

Objectives

The objective of PART is to compare the effectiveness of primary ETI versus primary LT airway management strategies upon 72-hour survival after OHCA.

Design

Participating EMS agencies will be clustered randomized to airway management with primary ETI (control) or primary LT insertion (intervention), with periodic crossover to the other arm.

Setting

PART will include participation by approximately 30 ground US EMS agencies associated with the Alabama, Dallas, Milwaukee, Pittsburgh and Portland Regional Clinical Centers of the Resuscitation Outcomes Consortium. (Appendix 1)

Patient Population (Inclusion/Exclusion Criteria)

PART will enroll adult (age ≥ 18 years or per local interpretation), non-traumatic OHCA requiring bag-valve-mask ventilation. If a subject receives bag-valve-mask ventilation but not ETI or SGA, he/she will be included in the study per intention-to-treat principles, regardless of recovery of consciousness. The trial will include EMS-witnessed arrests as well as patients experiencing recurrent OHCA during the same care episode. PART will exclude subjects that receive initial clinical care by non-trial EMS agencies with ETI or SGA insertion capabilities. Detailed inclusion and exclusion criteria are listed in Table 1.

Trial Interventions

PART will compare two interventions (Figure 2):

- **Initial Endotracheal Intubation (Control arm)** - EMS personnel will perform orotracheal intubation for initial advanced airway management attempts. Alternate ETI approaches (–e.g., nasotracheal intubation, digital intubation, video laryngoscopy) will not be permitted for the initial intubation effort.
- **Initial Laryngeal Tube Insertion (Intervention arm)** - EMS personnel will perform LT insertion for initial advanced airway management attempts. The trial will focus on LT insertion since it is the most common out-of-hospital SGA used in the United States. Other SGA (–e.g., Combitube, laryngeal mask airway and i-gel) will not be permitted for initial advanced airway management.^{27,28} The limited funding for the trial precludes evaluation of other SGA types.

In keeping with the pragmatic design of the trial, PART will not restrict other aspects of airway management and OHCA care. If initial ETI/LT insertion efforts are unsuccessful in either arm, EMS personnel may perform “rescue” airway management using any available airway technique, including bag-valve-mask ventilation, ETI (including alternate ETI techniques such as video laryngoscopy), insertion of LT insertion or another SGA device, needle jet ventilation or cricothyroidotomy. PART will not dictate or limit the number of ET tube or LT insertion attempts. PART will not restrict the use of neuromuscular blocking (NMB) agents to facilitate ETI. EMS personnel will verify correct ET tube or LT placement according to local protocols. EMS personnel will secure the airway device in place and reassess its placement per local protocol. EMS personnel will follow existing local protocols for OHCA care, including the timing, sequence and method of ETI or LT insertion, chest compressions, rhythm assessment, shock delivery, vascular access, drug administration and termination of resuscitation.

Rationale for the Absence of a BVM-Only Arm—Some observational studies suggest higher survival with BVM than ETI or SGA.¹⁸ However, in preparation for PART, ROC EMS professionals perceived a need for some degree of active ventilatory support and expressed discomfort with a BVM-only arm. Therefore, consistent with the pragmatic design of the trial, PART will not include a BVM-only arm.

Integration with Airway Management by Basic-Level EMS Personnel—Many EMS system use tiered response strategies, with separate basic and advanced life support (BLS/ALS) units jointly responding to OHCA incidents. Most BLS personnel in the United States do not perform ETI or LT insertion; in these cases arriving ALS personnel will carry out randomization and trial procedures. However, select BLS EMS agencies are trained in LT insertion; in these cases, BLS units will be integrated into the trial protocol.^{29,30} When assigned to the control arm, these BLS units will perform BVM ventilation. When assigned to the intervention arm, these BLS personnel will perform initial LT insertion. The cluster randomized design of the study will ensure that responding ALS and BLS units are assigned to the same study arm. PART does *not* require BLS EMS agencies to implement LT use.

Given the configuration and practice patterns of the trial EMS agencies, it is unlikely that a BLS unit will provide OHCA care without an accompanying ALS unit.

Hospital Care—PART will not dictate airway management care by receiving EDs nor post-arrest care such as Therapeutic Hypothermia/Targeted Temperature Management or percutaneous coronary intervention.³¹

Randomization

PART will use cluster randomization with periodic crossover. Each regional site will be subdivided into multiple clusters by EMS agency. Each cluster will be block randomized to one of the study interventions, with crossover between intervention assignments occurring at least twice per year. If more than one participating EMS agency is present on scene, the first arriving EMS unit participating in the trial will determine the study treatment assignment. Because the type of airway device used by EMS personnel cannot be concealed, blinding of the treatment assignment is not possible.

EMS agencies participating in PART have had extensive experience with cluster-crossover randomization and expressed comfort with this strategy.^{32–34} EMS personnel perceived event-level (e.g, blinded envelope or telemetry) and alternate-day randomization as adding unacceptable complexity and delays. While used in a prior trial, blinded airway equipment pouches were deemed impractical given the range of different airway equipment currently carried by EMS units.³⁵

Outcome Measures

Primary Outcome—The primary outcome of the trial is 72-hour hospital survival, defined as patient status (alive/dead) at 72 hours after the onset of cardiac arrest. (Table 2) In cases of field resuscitation termination, vital status will be determined from EMS records. If hospital records cannot be accessed, the trial will determine vital status from public death records.

Traditional OHCA trial endpoints such as neurologically-intact survival to hospital discharge require extremely large sample sizes (on the order of 10,000–20,000 subjects) to demonstrate small but clinically meaningful outcome differences.^{36,37} The available grant support did not allow for the execution of such a large trial. Prior OHCA trials have used return of spontaneous circulation, survival to hospital admission, and 24-hour survival as primary outcomes, but this strategy overlooks post-arrest care elements common in current practice: a) the delivery of therapeutic hypothermia (targeted temperature management), which typically requires 48–72 hours, b) early percutaneous coronary intervention, and c) delay of neurologic assessment and withdraw of care decisions until at least 72 hours after the cardiac arrest event.^{38–40}

The specification of 72-hour survival as the primary trial outcome afforded many advantages. Compared with survival to hospital discharge, the use of 72-hour survival as the primary outcome allowed for a smaller trial sample size. In contrast to return of spontaneous circulation, survival to hospital admission, and 24-hour survival, 72-hour survival accommodated for the delivery of therapeutic hypothermia, early percutaneous coronary

intervention, and delay of neurologic assessment. Furthermore, some clinicians believe that out-of-hospital interventions have more plausible connections with proximal outcomes (such as 72-hour survival) rather than later outcomes (such as neurologically intact survival to hospital discharge) which may be influenced by post-resuscitation care practices at receiving hospitals. In a prior study of 1,496 adult OHCA, we observed that the vast majority of OHCA deaths (90.6%) occurred within three days, affirming that the vast majority of OHCA deaths would be observed during this timeframe.⁴¹

Secondary Outcomes and Other Endpoints—Secondary trial outcomes include a) return of spontaneous circulation (ROSC), defined as the presence of palpable pulses upon ED arrival, b) survival to hospital discharge, and c) neurologically intact survival to hospital discharge, defined as a Modified Ranking Score ≤ 3 . (Table 2) The trial will also assess airway management process measures and safety events.

CPR Process and Other Physiologic Measures—Pragmatic trials traditionally focus on the outcomes of study interventions rather than the underlying mechanisms. Physiologic mechanisms hypothesized to influence OHCA outcomes following advanced airway management include CPR interruptions, hyperventilation, and carotid artery impingement.^{8,9,42,43} All participating ROC EMS units have automated external defibrillators (AED) and/or manual monitor/defibrillators capable of monitoring delivered chest compressions and ventilations, allowing estimates of chest compression rate, interruptions, fraction, and depth, and ventilation rate; these data will be archived for future analysis.^{44–47} The available grant funds are insufficient to support processing, cleaning and interpretation of CPR process files. While Segal, et al. highlighted potential carotid artery impingement from ET tube and SGAs devices in a porcine cardiac arrest model, there are currently no available methods to measure these adverse events in human OHCA.⁴²

Analysis Plan

Data analyses will include both intention-to-treat and as-treated comparisons. The intention-to-treat comparison will analyze subjects according to their assigned treatment arm (initial-ETI vs. initial-LT).

To assess the impact of deviations from random assignment, the trial will include as-treated comparison based upon the initial attempted advanced airway technique (ETI or LT), regardless of insertion success. A second as-treated comparison will consider the final result of EMS airway management efforts: a) ETI, b) LT, c) BVM, and d) other airway technique. In cases where rescuers use only BVM (without resorting to ETI or LT insertion), the subject will be retained in the assigned randomization. In cases where rescuers use an initial advanced airway technique other than ETI or LT, the subject will be excluded from further analysis.

Since randomization includes all eligible OHCA patients, the primary analysis will not stratify by initial cardiac rhythm. However, consistent with prior OHCA trials, the trial results will be stratified by *a priori* defined subgroups (Table 3).^{32,33} The analysis will use multiple imputation to address cases with missing data.

Sample Size Estimate and Interim Monitoring Plan

The trial sample size estimate is based upon the primary outcome of 72-hour survival. (Appendix 2) In the prior ROC PRIMED study, baseline 72-hour survival was 13.7%, with a 5.1% absolute difference in 72-hour survival between ETI (16.2%) and SGA (11.1%).^{32,33} To allow for potential confounders, we estimated 4.5% to represent the minimum clinically significant difference in 72-hour survival. We designed the trial to have 85% power to detect a 4.5% difference in 72-hour survival, assuming an overall significance level of 0.05 (adjusted for interim analyses) and accommodating up to a 5% loss of precision due to cluster randomization with crossover. The required minimum sample size is 2,612 subjects (1,306 per group). To allow for possible subject withdrawal and loss to follow-up, PART will aim to enroll a total of 3,000 subjects. Stopping boundaries for the trial will follow asymmetric two-sided designs based upon the unified family of group sequential stopping rules.^{48,49} (Appendix 1) The trial will encompass four total analyses (three interim + one final).

Data Collection

The ROC “Cardiac Epistry” epidemiological database contains information on all OHCA treated by consortium EMS agencies from 2005–2015.⁵⁰ The database is web-based, allowing data entry from multiple sites, and contains standard error-checking, security and encryption measures. PART will use the Cardiac Epistry for trial data collection.

Training

All participating EMS units will undergo training in the execution of the PART protocol. Training will consist of a didactic session followed by hands-on scenario-based training. Prior studies highlight the influence of paramedic airway management experience upon patient outcomes.^{51,52} Characterization of paramedic lifetime experience in airway management is difficult. The type and quantity of airway management training provided to paramedics also varies nationally. Consistent with the pragmatic nature of the trial, EMS personnel will execute PART using their standard airway management training practices. The trial will not provide supplemental ETI or LT training on cadavers or live hospital patients.

Ethical Considerations

PART will take place under US federal rules for exception from informed consent for emergency research (EFIC).^{53,54} In conformance with EFIC rules, measures to inform and protect potential subjects will include; a) community consultation, b) public disclosure, c) independent data monitoring, d) notification of a legally authorized representative or family members of a subject’s enrollment in the trial as soon as feasible, with opportunity to discontinue trial participation, and e) provision of an opt-out mechanism. Consistent with prior ROC experience, PART sites will conduct a range of activities to accomplish community consultation and public disclosure, community meetings, random-digit telephone surveys, and the use of internet social media.^{55–58}

Trial Safety, Monitoring and Oversight

Comprised of lead investigators, representatives from NHLBI and appointed site representatives, a study monitoring committee will provide regular oversight of trial enrollment. A data safety and monitoring board (DSMB) appointed by the National Institutes of Health will conduct periodic independent assessments of trial progress, using data from interim analyses to formulate recommendations on trial continuation or termination.

Duration of the Study

Each month, the participating EMS agencies collectively treat an estimated 155 OHCA requiring advanced airway management or ventilatory assistance. Therefore, PART will require approximately 2 years to enroll the requisite number of subjects (n=3,000). PART enrollment is anticipated to take place between December 2015 and October 2017.

DISCUSSION

PART will provide information to guide the optimal advanced airway management strategy in OHCA resuscitation. Should PART identify better outcomes with LT insertion than ETI, EMS agencies and practitioners may adopt OHCA protocols favoring LT insertion. Conversely, should PART identify better outcomes with ETI than LT, this finding would affirm the current use of ETI as the primary OHCA approach. Should the trial be unable to detect an outcome difference between ETI and LT, the appropriate clinical interpretation will be less clear. In the latter case, medical directors may potentially select the advanced airway strategies best suited to the skill set and training resources available to individual EMS agencies.

The most prominent feature of PART is the use of 72-hour survival as the primary outcome, a measure reflecting the pragmatic design of the trial. OHCA trials are traditionally designed to detect small differences in absolute survival (<1%), consequently requiring 20,000 or more subjects. The recently completed ROC Continuous Chest Compressions Trial enrolled almost 24,000 subjects.^{36,37} By focusing on the more proximal outcome 72-hour survival, PART will require <3,000 enrolled subjects. The focus on 72-hour survival supports the pragmatic notion that prehospital interventions may be more closely aligned with proximal than more distant outcomes. The lower required enrollment is consistent with NIH's objective of supporting efficient trials with pragmatic findings that can be rapidly implemented into practice.^{59,60}

In a parallel effort in the United Kingdom, Bengert, et al. have completed the pilot REVIVE-Airways Trial and are currently carrying out the Airways-2 Trial.⁶¹ Completed in 2013, REVIVE-Airways included specially trained study paramedics who were randomly assigned to use i-gel SGA, Laryngeal Mask Airway (LMA) or "usual care" (ETI) when treating OHCA.⁶¹ The study successfully enrolled 615 patients (i-gel 232, LMA 174, ETI 209) during a one-year period, demonstrating the feasibility of randomizing airway devices in the prehospital setting. In a larger follow-up effort, the authors are actively enrolling subjects in

the Airways-2 Trial, which randomizes paramedics to adult OHCA treatment with i-gel or usual care with ETI.

There are key distinctions between PART and Airways-2. While Airways-2 will evaluate the i-gel, which is widely used in the United Kingdom, PART will test the LT, which is the most widely used prehospital SGA in the US. PART will cluster randomize by EMS agency, capturing all eligible adult OHCA treated by participating agencies. Airways-2 will randomize by paramedic, excluding OHCA not treated by study paramedics. PART will enroll 3,000 subjects to detect 72-hour survival. Airways-2 will enroll 9,000 subjects to detect survival to hospital discharge. The results of PART and Airways-2 will offer important complementary information to collectively guide OHCA airway management practices.

Acknowledgments

FUNDING STATEMENT

This work is supported by UH2/UH3-HL125163 from the National Heart, Lung and Blood Institute (NHLBI). In addition, the ROC data coordinating center and sites are supported through a series of cooperative agreements through the NHLBI (5U01 HL077863-University of Washington Data Coordinating Center, HL077866-Medical College of Wisconsin, HL077871-University of Pittsburgh, HL077873-Oregon Health and Science University, HL077881-University of Alabama at Birmingham, HL077887-University of Texas Southwestern Medical Center/Dallas).

ROLE OF THE FUNDING SOURCE

None.

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APPENDIX 1

EMS agencies participating in PART. EMS=emergency medical services. ALS=advanced life support. BLS=basic life support. LT=laryngeal tube

Regional Coordinating Center	EMS Agency	Location	Care Level of Responding Units	LT Use by BLS Personnel
Alabama	Birmingham Fire and Rescue Service	Birmingham, AL	ALS and BLS	No

Regional Coordinating Center	EMS Agency	Location	Care Level of Responding Units	LT Use by BLS Personnel
Alabama	Bessemer Fire Department	Bessemer, AL	ALS and BLS	No
Dallas	Garland Fire Department	Garland, TX	ALS	N/A
Dallas	Irving Fire Department	Irving, TX	ALS	N/A
Dallas	Mesquite Fire Department	Mesquite, TX	ALS	N/A
Dallas	MedStar Mobile Healthcare	Fort Worth, TX	ALS and BLS	Yes
Milwaukee	City of Milwaukee Fire Department	Milwaukee, WI	ALS and BLS	Yes
Milwaukee	North Shore Fire Department	Brown Deer, WI	ALS and BLS	Yes
Milwaukee	West Allis Fire Department	West Allis, WI	ALS and BLS	Yes
Milwaukee	Wauwatosa Fire Department	Wauwatosa, WI	ALS and BLS	Yes
Milwaukee	Oak Creek Fire Department	Oak Creek, WI	ALS and BLS	Yes
Milwaukee	Franklin Fire Department	Franklin, WI	ALS and BLS	Yes
Milwaukee	South Milwaukee Fire Department	South Milwaukee, WI	ALS and BLS	Yes
Milwaukee	Greenfield Fire Department	Greenfield, WI	ALS and BLS	Yes
Milwaukee	Cudahy Fire Department	Cudahy, WI	BLS	Yes
Milwaukee	Hales Corners Fire Department	Hales Corners, WI	BLS	Yes
Milwaukee	Greendale Fire Department	Greendale, WI	ALS and BLS	Yes
Milwaukee	St. Francis Fire Department	St. Francis, WI	BLS	Yes
Pittsburgh	Medical Rescue Team South Authority	Mt. Lebanon, PA	ALS and BLS	No
Pittsburgh	Tri-Community South EMS	Bethel Park, PA	ALS	N/A
Pittsburgh	Scott Township EMS	Scott Township, PA	ALS and BLS	No
Pittsburgh	Kirwan Heights Fire Department	Bridgeville, PA	ALS and BLS	No
Portland	Clackamas Fire District # 1	Clackamas County, OR	ALS and BLS	Yes
Portland	Hillsboro Fire Department	Hillsboro, OR	ALS and BLS	Yes
Portland	Lake Oswego Fire	Lake Oswego, OR	ALS and BLS	Yes
Portland	Skamania County EMS	Stevenson, WA	ALS and BLS	Yes
Portland	Tualatin Valley Fire & Rescue	Tigard, OR	ALS and BLS	No
Portland	Metro West Ambulance	Hillsboro, OR	ALS	No

APPENDIX 2

Estimates of sample size and interim stopping boundaries. Because ETI is more complex and resource intensive than LT insertion, boundaries for early termination were chosen to have a higher superiority threshold for ETI over LT (–e.g., 12.5% absolute 72-hour survival difference in favor of ETI at first interim analysis) than for LT over ETI (–e.g., 10.8% absolute 72-hour survival difference in favor of LT at first interim analysis). The study does not include any futility boundaries because obtaining estimates in either direction will be considered informative.

	Statistical Power (1- β)		
Effect Size (Absolute Difference)	80%	85%	90%
4.0%	2,856	3,266	3,892
4.5%	2,284	2,612	3,112
5.0%	1,872	2,142	2,550
Sample Size Estimates Effect sizes based upon 13.7% baseline 72-hour survival.			

			Lower Stopping Boundary (LT Better)			
Analysis	Cum. Sample Size	Prop. Max Stat Info	Absolute Difference	Adjusted Difference	95% Confidence Interval	P-value
1	654	0.25	-0.108	-0.098	(-0.154, -0.041)	0.001
2	1,306	0.50	-0.102	-0.092	(-0.135, -0.053)	<0.001
3	1,958	0.75	-0.092	-0.084	(-0.120, -0.052)	<0.001
4	2,612	1.00	-0.029	-0.029	(-0.059, 0.000)	0.050

			Upper Stopping Boundary (ETI Better)			
Analysis	Cum. Sample Size	Prop. Max Stat Info	Absolute Difference	Adjusted Difference	95% Confidence Interval	P-value
1	654	0.25	0.125	0.116	(0.058, 0.172)	<0.001
2	1,306	0.50	0.118	0.109	(0.069, 0.151)	<0.001
3	1,958	0.75	0.106	0.099	(0.066, 0.135)	<0.001
4	2,612	1.00	0.029	0.029	(0.000, 0.059)	0.050
Interim Stopping Boundaries for 72-Hour Survival

FIGURE 1.
Resuscitation Outcomes Consortium centers participating in PART.

FIGURE 2.

Overview of PART protocol. ETI = endotracheal intubation. LT = laryngeal tube. BVM = bag-valve-mask ventilation. EMS = Emergency Medical Services.

TABLE 1

Trial inclusion and exclusion criteria. ETI = endotracheal intubation. LT = laryngeal tube. EMS = emergency medical services.

Inclusion Criteria

- Adult (age ≥ 18 years or per local interpretation), non-traumatic OHCA
- Treated by EMS personnel
- Requiring advanced airway insertion (ETI, LT) or ventilatory support (bag-valve-mask ventilation)

Exclusion Criteria

- Known pregnant women
 - Known prisoners
 - Major facial trauma
 - Major bleeding or exsanguination
 - ET tube, LT or other advanced airway insertion prior to ROC EMS arrival
 - Pre-existing tracheostomy
 - Obvious asphyxial cardiac arrest (choking or hanging)
 - Left ventricular assist device (LVAD) or total artificial heart (TAH),
 - Pre-existing “do-not-attempt-resuscitation” (DNAR) orders
 - Inter-facility transports
 - Presence of a “do not enroll” bracelet
 - Initial care by non-trial EMS agency capable of performing ETI, LT or other advanced airway Insertion
-

TABLE 2

Study outcomes. ETI = endotracheal intubation. LT = laryngeal tube. EMS = emergency medical services.

Outcome Measure	Definition or Criteria
Primary Outcome	- Defined as vital status (alive/dead) 72-hours after onset of cardiac arrest or initiation of resuscitation.
- 72-hour survival	
Secondary Outcomes	- Defined as presence of pulses on Emergency Department arrival.
- Return of spontaneous circulation	- Defined as vital status (alive/dead) on hospital discharge.
- Survival to hospital discharge	- Defined as Modified Rankin Score (MRS) ≤ 3 on hospital discharge. Dead defined as MRS=6.
- Neurologically-intact survival to hospital discharge	
Airway Management Process and Adverse Events	- ETI-first vs LT-first
- Sequence of ETI/LT attempts	- Multiple attempts defined as ≥ 3 insertion attempts
- Number of ETI/LT attempts	- Details Emergency Department management of EMS-placed airway.
- Success of ETI/LT insertion efforts	- Unrecognized EMS endotracheal tube placement in the esophagus or hypopharynx, or displacement of a correctly placed ET tube. Does not include instances of immediately recognized ET tube misplacement. Does not include ED airway misplacements.
- Successful airway insertion time, or time advanced airway efforts abandoned	- Inadequate ventilation prompting EMS to change airway device
- Initial airway course in receiving Emergency Department	- Limited to first 24 hours of hospitalization.
- Unrecognized airway misplacement or dislodgement	- Determined from hospital records.
- Inadequate ventilation	- Determined from first in Emergency Department chest x-ray.
- Airway swelling or edema	- Determined from radiology interpretation of chest x-rays for first 72-hours of hospitalization
- Oropharyngeal or hypopharyngeal injury	
- Pneumothorax	
- Pneumonia and aspiration pneumonitis	

TABLE 3

A priori defined analytic subgroups.

Initial cardiac rhythm (shockable vs. non-shockable)
Bystander witnessed OHCA (yes vs. no)
Emergency medical services unit response time (dispatch call to arrival on-scene: <10 vs. ≥ 10 mins)
Basic life support unit capability of performing LT insertion (yes vs. no)
Time of airway placement after rescuer arrival (early [<10 minutes] vs. later [≥ 10 minutes])
Airway placement prior to or after return of spontaneous circulation
Use of neuromuscular blocking agent before or during airway insertion efforts (yes vs no)
Age (<65 vs. ≥ 65 years)

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