Full Title:

Randomised comparison of the effectiveness of the laryngeal mask airway supreme, i-gel and current practice in the initial airway management of out of hospital cardiac arrest: a feasibility study

Short Running Title: LMAS vs i-gel vs current practice in OHCA

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Summary

Background

The best initial approach to advanced airway management during out of hospital cardiac arrest (OHCA) is unknown. The traditional role of tracheal intubation has been challenged by the introduction of supraglottic airway devices (SGAs), but there is contradictory evidence from observational studies. We assessed the feasibility of a cluster-randomised trial to compare the i-gel SGA versus the laryngeal mask airway supreme (LMAS) versus current practice during OHCA.

Methods

Cluster-randomised trial in a single ambulance service in England, with individual paramedics as the unit of randomisation. Consenting paramedics were randomised to use either the i-gel or the LMAS or usual practice for all cases of non-traumatic adult OHCA that they attended over a 12-month period. The primary outcome was study feasibility, including paramedic and patient recruitment and protocol adherence. Secondary outcomes included survival to hospital discharge and 90 days.

Results

Of the 535 paramedics approached, 184 consented and 171 attended study training. Each paramedic attended between 0 and 11 patients (median 3; interquartile range 2-5). We recruited 615 patients at a constant rate, although the LMAS arm was suspended in the final two months following three adverse incidents. The study protocol was adhered to in 80% of cases. Patient characteristics were similar in the three study arms, and there were no differences in secondary outcomes.

Conclusions

We have shown that a prospective trial of alternative airway management strategies in OHCA, cluster randomised by paramedic, is feasible.

MeSH Key Words

Cardiopulmonary resuscitation; heart arrest; mortality; resuscitation

Clinical Trial Registration.

Registered on the International Standard Randomised Controlled Trial Registry (ISRCTN: 18528625)

http://www.controlled-trials.com/ISRCTN18528625

Introduction

In the United Kingdom (UK) there are 118 out of hospital cardiac arrests (OHCAs) per 100,000 population per annum,[1] and the UK ambulance service attends 60,000 such patients each year.[2] Approximately 7% survive to hospital discharge.[3]

Immediate cardiopulmonary resuscitation (CPR) following cardiac arrest improves survival rates.[4] Effective ventilation is an essential component of CPR,[5] and is associated with both return of spontaneous circulation (ROSC) and neurological recovery.[6] However, what constitutes effective ventilation is uncertain.[7]

Traditionally, tracheal intubation has been viewed as the best airway management during OHCA.[8] However, this assumption has never been tested prospectively,[9] and pre-hospital intubation attempts by paramedics are associated with important complications: interruptions in chest compressions, unrecognised oesophageal intubation (particularly when end-tidal carbon dioxide monitoring is not used), compromised oxygenation and delays in accessing definitive care.[10 11]

Supraglottic airway devices (SGAs) are an alternative to intubation. They are faster and easier to insert and may reduce the complications associated with tracheal intubation.[12] SGAs are used safely and effectively in many hospital procedures;[13-15] however their safety and efficacy out of hospital has not been well studied. The risk of regurgitation is higher during OHCA,[16 17] and SGAs may dislodge more frequently than tracheal tubes.

The Joint Royal Colleges Ambulance Liaison Committee (JRCALC) has recommended that ambulance services in the UK consider SGAs as an alternative to tracheal intubation.[18] SGAs are now used routinely in many UK ambulance services.[19] The 2013/14 London Ambulance Service report documented 1354/1637 (82.7%) successful OHCA intubations and 2674/2954 (90.5%) successful SGA placements.[20]

Equipoise between the two techniques has led to calls for a large randomised clinical trial (RCT) comparing SGAs with tracheal intubation.[21 22] However, such a trial is both logistically and ethically challenging, with considerable uncertainty as to whether it could be completed successfully. Some previous randomised trials involving paramedics have been unsuccessful as a result of poor compliance and patient crossover,[23] and no randomised trial of tracheal intubation versus SGAs has ever been completed in cardiac arrest. Furthermore, several SGAs are available, but the optimal device during OHCA is unknown. Therefore, before proceeding to a large-scale and costly randomised trial, recruiting many thousands of patients, it was necessary to demonstrate that our proposed study design was feasible, to develop and refine the methodology and identify the optimal SGA for use in subsequent research.

Our hypothesis was that a cluster randomised trial to compare the ventilation success of two SGAs to usual practice during the initial airway management of OHCA in an English ambulance service is feasible. Our primary objective was therefore to assess the feasibility of a prospective cluster randomised trial to compare the ventilation success of two second generation SGAs: the i-gel (Intersurgical; Wokingham, UK) and the laryngeal mask airway supreme (LMAS) (LMA/Teleflex; San Diego, USA) to usual practice (principally tracheal intubation), as the initial approach to advanced airway management during OHCA. The secondary objectives were to estimate the intra-class correlation coefficient for paramedic clusters to establish the variance arising from a cluster randomised design, and to describe the clinical outcomes of the i-gel versus LMAS versus current practice during the initial management of OHCA, in terms of insertion and ventilation success, return of spontaneous circulation (ROSC), survival to hospital discharge, and survival, neurocognitive function and quality of life 90 days after OHCA.

Methods

The study methods have been described previously.[24] In summary, we completed a feasibility study, using a cluster randomised design, to compare the initial use of the i-gel and LMAS with current practice during resuscitation for OHCA. The study setting was a single ambulance service in Southwest England, covering an urban and semi-rural population of approximately 2 million people.

Randomisation

We chose a cluster randomised design because an individually randomised design would require participating paramedics to carry and use all devices, increasing the risk that they would not use the device to which a patient had been allocated. It is also logistically challenging to randomise individual patients during the initial management of OHCA, when immediate patient care and effective CPR is the priority.

We therefore selected cluster randomisation by paramedic, seeking volunteers from the Great Western Ambulance Service NHS Trust (now South Western Ambulance Service NHS Foundation Trust: SWAST). Paramedics were eligible if they were engaged in regular operational duties, were not employed in a specialist role and volunteered to take part. Participating paramedics were randomly allocated to one of the three study arms (i-gel, LMAS or current practice) through an independent computer-generated process undertaken by the trial statistician, and with full concealment. Randomisation was stratified by years of operational experience ($\leq$ 4 years, or > 4 years full time experience) and by rural or urban location of the paramedic's base ambulance station.

Paramedic Training

Following written informed consent participating paramedics were invited to attend a structured training session lasting 120 minutes: 60 minutes of generic training on resuscitation, airway management and trial procedures, and an additional 60 minutes of airway training specific to the

study arm, with competence confirmed through the administration of a brief standardised verbal and practical assessment. Paramedics randomised to the i-gel or LMAS arms were issued with a personal supply of the relevant device, and were required to account for each use. Paramedics randomised to routine care were instructed to continue with their normal practice, which included the choice of bag-mask ventilation, a single-use disposable Laryngeal Mask Airway (AMBU Auraonce; Ballerup, Denmark) or tracheal intubation.

Patient Eligibility

Patients were eligible for enrolment in the study if they were in cardiac arrest outside hospital, attended by a paramedic enrolled in the trial, attempted resuscitation was deemed appropriate according to Joint Royal Colleges Ambulance Liaison Committee (JRCALC) guidelines, and the patient was known or believed to be 18 years or older.

Exclusion criteria were cardiac arrest caused by trauma, estimated patient weight less than 50 kg, mouth opening less than 2 cm, patient detained by Her Majesty's Prison Service, or previously recruited to the same study.

The first paramedic participating in the study to arrive on scene determined the allocation of the patient, with analysis undertaken on an intention to treat basis.

Blinding

Because of the nature of the intervention, ambulance clinicians could not be blinded. Control room personnel were blinded to the allocation of paramedics, which ensured there was no bias in dispatch. Patients were unaware of their allocation throughout the trial. Outcome assessment was carried out by an individual blinded to study allocation.

Study Procedures

Participating paramedics were instructed to deliver standard resuscitation protocols to all patients in accordance with Resuscitation Council (UK) guidelines, with the exception that the allocated approach to initial airway management was used whenever possible.

For the i-gel and LMAS arms, the SGA was inserted at the first opportunity without interrupting cardiopulmonary resuscitation (CPR), and an attempt made to ventilate the lungs at a rate of approximately 10 breaths a minute while compressions were ongoing. If ventilation was deemed inadequate (no chest rise observed), chest compressions were paused to enable ventilation of the lungs using a chest compression to ventilation ratio of 30:2.

The SGAs were inserted according to the manufacturer's instructions. Paramedics made a maximum of three attempts to place their allocated SGA, and were instructed to take no more than 30 seconds for each attempt. If a paramedic was unsuccessful at the third attempt, they switched to whatever alternative technique they deemed to be in the best interests of the patient.

Adequate ventilation with a device was defined as visible chest rise with each breath. To ensure that all eligible OHCA patients were included in the study daily searches of the ambulance computer-aided despatch (CAD) system were undertaken to identify possible OHCAs, and the study records were regularly reconciled with routinely collected data relating to all OHCA patients. At the end of the trial all SGAs were collected and accounted for, to ensure that no device was used outside the study protocol.

Sample Size Calculation

In this feasibility study a formal calculation of power was not carried out, but an analysis of the expected number of paramedics who would attend two or more eligible events in a 12-month period was completed, estimating the events to occur randomly throughout the sample and following a Poisson distribution. This indicated that 7% of paramedics would not be expected to attend any

suitable patients in 12 months, and 10% would attend only one event. Therefore, in order to ensure that at least 30 paramedics in each arm attended at least two events, and to allow for some paramedics drop out, we aimed to recruit 50 paramedics to each trial arm.

Clinical Outcome Measures

Return of spontaneous circulation (ROSC) was reported by participating paramedics, and confirmed by review of hospital notes. Survival to hospital admission and survival to hospital discharge were confirmed by review of hospital notes, and by direct contact with the patient or their consultee during the consent process. Survival to 90 days following OHCA was confirmed by contact with the patient's general practitioner, prior to follow-up data collection by a researcher, blinded to treatment allocation, in the patient's home.

At 90 days the Cambridge neuropsychological test automated battery (CANTAB) was administered: a computerised touch-screen system that objectively measures a range of cognitive functions.[25] This tool has been previously used to assess cognitive function in OHCA survivors.[26] The Delayed Matching to Samples (DMS) test was chosen to assess short-term recognition memory. The total correct responses and correct responses on the 0 and 12s delay conditions were reported.[26] Quality of life (QoL) in survivors was measured using the Depression, Anxiety and Stress Scale and the Short Form-36 (SF-36) questionnaire.[27 28]

Ethical Considerations

OHCA is unpredictable. Within seconds of cardiac arrest a person becomes unconscious and thus incapacitated. In this situation it is impractical to consult another person without placing the potential participant at risk of harm from delaying treatment. Therefore, it was not possible to seek consent before enrolment and intervention, and an OHCA patient was considered to have been enrolled in the trial at the time of their cardiac arrest if they met the eligibility criteria and were attended by a participating paramedic. Consent to continue with follow-up was sought from

surviving patients once they had regained capacity in hospital. Alternatively, if the patient survived but did not have capacity, an opinion was sought from a consultee.

We did not seek to inform the relatives of patients who died soon after OHCA. Our patient forum was of the view that to inform relatives of the study, following a very recent bereavement, would serve no useful purpose and would only lead to unnecessary distress.

These processes were approved by the Cambridge Central NHS Research Ethics Committee, which has specific expertise in trials of medical devices in incapacitated adults.

The trial was registered (ISRCTN: 18528625). The contribution of the manufacturers of the SGAs was limited to confirming that the training of paramedics in the use of the devices conformed to their recommended guidelines. These manufacturers had no role in supplying devices or the design, funding, conduct, analysis or reporting of the trial.

Results

Of 535 eligible paramedics, 212 (40%) expressed an interest and 184 (35%) consented to participate. 171 (32%) attended training and were eligible to enrol patients, with 9 of these withdrawing during the study. Reasons for withdrawal were: maternity leave (5); leaving the employing ambulance service (2); long-term sick leave (1); no reason given (1).

The number of eligible patients attended by each participating paramedic over 12 months ranged from 0 to 11. The median was 3 (interquartile range 2 to 5), and 9% of paramedics attended no OHCA patients. The intra-class correlation coefficient (ICC) for the outcome of survival to discharge by paramedic clusters was <0.001 (95% CI, 0.00 - 0.065), indicating very little variance attributable to the cluster randomised design.

During the 12-month study period 2,990 cardiac arrests occurred in the participating ambulance service, of which 2,375 (79%) were not eligible for inclusion. A CONSORT diagram is shown in Figure 1. By far the commonest reason for non-eligibility was no active resuscitation attempt, (1,615 patients; 54%). All eligible patients (n = 615) were enrolled and analysed on an intention to treat basis.

The total number of patients enrolled in each study arm was: i-gel 232 (38%); LMAS 174 (28%); usual practice 209 (34%). The LMAS arm was discontinued after 10 months because on three occasions ambulance staff were contaminated by blood and vomit ejected forcefully from the gastric drainage port of the LMAS during CPR. Otherwise, recruitment to the three trial arms was consistent throughout the study.

Protocol adherence by trial arm is shown in Table 1. Overall, the study protocol was adhered to in 80% of cases. In 16% the patient received no advanced airway management (often for legitimate reasons such as rapid early recovery) or the incorrect device initially, and in 4% of patients these data were missing.

Baseline characteristics for the three trial arms are shown in Table 2. First attempt placement success for the i-gel was 79% (unable to insert: 4%, inadequate ventilation: 17%) and for the LMAS was 75% (unable to insert: 4%, inadequate ventilation: 21%). Overall, tracheal intubation was attempted in 46% of enrolled patients (267/584), and was successful on the first attempt in 85%. Other clinical outcomes, including survival to hospital discharge and survival to 90 days, are shown in Table 3. Neurocognitive outcomes are shown in Table 4, and quality of life outcomes are shown in Table 5.

Discussion

We have demonstrated that it is possible to complete a randomised trial of alternative airway management strategies during OHCA, successfully recruiting and randomising paramedics and enrolling and following-up patients. Recruitment of both paramedics and patients exceeded our pre-determined targets, and there was consistent recruitment with good protocol compliance. We did not show a difference in survival, neurocognitive function or quality of life between the three study arms, but the study was not powered sufficiently to detect clinically significant differences in these secondary outcomes.

Initial airway management is one of the most controversial aspects of OHCA. Registry data have demonstrated an association between bag-mask ventilation and improved outcomes when compared with both SGAs and tracheal intubation,[29-32] whereas a recent meta-analysis has shown that tracheal intubation was associated with better outcomes than SGAs.[33]

Paramedic dropout was around 5% per year, and the intra-class correlation coefficient (ICC) for paramedic clusters had a value of <0.001, which means that the variability between paramedics was low compared with the variability between the patients treated by a paramedic. This suggests that cluster randomisation by paramedic was close to individual patient randomisation, and reflects the fact that the number of patients treated by each paramedic was relatively small (median 3).

Following inadvertent contamination of ambulance staff in three cases, the LMAS arm was discontinued after 10 months. These three events were reported as adverse incidents, and also in a subsequently published letter.[34] The manufacturer of the LMAS responded suggesting that ambulance staff should ensure full personal protection, and that ejection of gastric contents indicated correct functioning of the device.[35] However, confidence in the LMAS was undermined and recruitment to this arm of the trial discontinued on the direction of the trial sponsor. Compliance with the LMAS was lower than with the i-gel, and paramedic feedback favoured the i-gel device.

Further evidence of the effective use of the i-gel during OHCA in Europe was published while this study was in progress.[19 36] We have therefore decided to use the i-gel in future studies.

We recruited 45% of all eligible patients who underwent resuscitation. No patient was lost to follow up, and the arrest characteristics of resuscitated patients who were enrolled and not enrolled in the study were very similar (data not shown). The baseline characteristics compared in Table 2 are well matched, and suggest that randomisation was effective. The rates of ROSC, hospital admission and survival to hospital discharge are similar to those reported from other parts of England.[20]

In the SGA groups, the first attempt placement success rate was 79% for the i-gel and 75% for the LMAS, which is slightly lower than some previous reports. One study documented a first attempt placement success rate of 90% for the i-gel in 70 OHCA patients in Germany (63 paramedics and 7 doctors).[37] Although the training provided in this study was similar to ours, the availability of other options is unclear. The only other prospective randomised trial of alternative airway management strategies in OHCA compared the i-gel with the Portex Soft Seal Laryngeal Mask (PSS-LM) in a total of 51 patients in Australia.[38] The authors report an insertion success rate of 90% for the i-gel and 57% for the PSS-LM (p=0.023), suggesting that the latter device is poorly suited to OHCA. In comparison, first pass success rates for the laryngeal tube (LT) have been reported recently as 72% and 83%.[39 40] We documented a first attempt tracheal intubation success rate of 85%. This is comparable with other reports of intubation success in cardiac arrest: tracheal intubation was achieved in three or fewer attempts in 91% of 628 OHCA patients in a Scottish study.[11]

Ongoing uncertainty in this area of practice has led to consistent calls for a RCT to determine which advanced airway is best in the initial management of OHCA,[15 35 36] and we are now progressing to a large-scale RCT of the i-gel versus tracheal intubation.

Limitations

This study has several weaknesses. We designed the study to avoid overlooking any eligible patients, and also to minimise bias, but given the cluster randomised design and the complexities of the clinical environment we cannot rule out the possibility that a degree of residual bias exists. Randomisation by patient would have been preferable, but was judged impractical and potentially unethical if it led to delays in care. We recruited only one third of all eligible paramedics, and since these were volunteers they may not be representative of the wider paramedic profession. The study was completed in a single UK ambulance service, and not all eligible patients were enrolled: therefore whilst the characteristics of enrolled and not enrolled patients were similar our results may not be generalizable to other regions or countries. The clinical outcomes were collected in an independent and blinded fashion, but some of the process outcomes (e.g. first attempt device placement success) were self-reported and the paramedics themselves were not blinded. The usual practice arm was not standardised, so although this represents a pragmatic comparison it consists of a range of practices including bag-mask ventilation alone and the use of a different SGA, as well as tracheal intubation.

Conclusion

We have demonstrated that a prospective randomised trial of alternative approaches to advanced airway management during adult non-traumatic OHCA is feasible in the UK, through the effective engagement of paramedics, and that a high degree of protocol compliance can be achieved. We found no differences in survival, neurocognitive function or quality of life between a supraglottic airway device and usual practice during OHCA. However the trial was insufficiently powered to detect important differences in these clinical outcomes. We are now proceeding to a large-scale RCT of the i-gel versus tracheal intubation in OHCA.

Declaration of Interests

No interests declared.

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Author's Contribution

JB: Study design and oversight, first draft of paper. DC: Paramedic recruitment and data collection, editing paper. SED: Follow-up data collection, data analysis, editing paper. RG: Study design and data analysis, editing paper. JPN: Study design, subject expertise, editing paper. MR: Paramedic and patient recruitment, data collection, editing paper. MT: Study design, paramedic training, subject expertise, editing paper. SV: Study design, trial management, data analysis, editing paper.

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	Adherent n (%)	Non-adherent n (%)	Missing Data n (%)
i-gel (n = 232)	172 (74)	51 (22)	9 (4)
LMAS (n = 174)	119 (68)	46 (26)	9 (5)
Usual practice (n = 209)	198 (95)	3 (1)	8 (4)
Total (n = 615)	489 (80)	100 (16)	26 (4)

Table 1: Protocol adherence by trial arm

Characteristic	i-gel (n = 232)	LMAS (n = 174)	Usual Practice (n = 209)
Age: years (mean, median (SD))	70, 73 (17.1)	71, 74 (15.5)	71, 75 (14.6)
Male: % (n/N)	64.6 (144/223)	61.2 (104/170)	58.6 (119/203)
Presumed cardiac cause: % (n/N)	94.2 (213/226)	97.1 (165/170)	97.1 (200/206)
OHCA at home address: % (n/N)	74.8% (169/226)	71.8% (122/170)	73.8% (152/206)
Witnessed:% (n/N)	32.3% (73/226)	30.0% (51/170)	35.1% (72/205)
Bystander CPR: % (n/N)	46.9% (106/226)	50.6% (86/170)	40.3% (83/206)

Table 2: Baseline characteristics of three trial arms. SD – standard deviation; LMAS – laryngeal mask airway supreme; OHCA – out of hospital cardiac arrest; CPR – cardiopulmonary resuscitation.

Outcome	i-gel % (n/N) n = 232	LMAS % (n/N) n = 174	Usual Practice % (n/N) n = 209
ROSC on hospital arrival	30.8 (70/227)	31.2 (53/170)	32.7 (67/205)
Admission to hospital	22.0 (50/227)	17.6 (30/170)	21.0 (43/205)
Survival to hospital discharge	10.3 (24/232)	8.0 (14/174)	9.1 (19/209)
Survival to 90 days	9.5 (22/232)	6.9 (12/174)	8.6 (18/209)

Table 3: Comparison of the clinical outcomes between the three trial arms. LMAS – laryngeal mask airway supreme; ROSC – return of spontaneous circulation.

CANTAB DMS	i-gel mean correct (SD) n = 14	LMAS mean correct (SD) n = 10	Usual Practice mean correct (SD) n = 10
All Delays	11.8 (2.4)	10.7 (1.6)	9.9 (2.0)
0 Second Delay	4.3 (1.0)	4.1 (1.0)	3.8 (1.0)
12 Second Delay	3.4 (1.5)	3.2 (0.9)	3.0 (1.3)

Table 4: Comparison of neurocognitive outcomes between the three trial arms. SD – standard deviation; *LMAS – laryngeal mask airway supreme; CANTAB - Cambridge neuropsychological test automated battery; DMS – delayed matching to samples. The maximum possible score was five for 0 second delay, five for 12 second delay, and fifteen for all delays. Seven patients declined to participate in this part of the study, and one patient with a pre-existing neurological deficit was excluded. Seven further patients were excluded from the DMS analyses because they were unable to complete the assessment.*

Quality of Life Measure	i-gel mean score (SD) n = 16	LMAS mean score (SD) n = 11	Usual Practice mean score (SD) n = 14
SF-36 Physical Component Score	43.9 (11.4)	41.5 (11.3)	49.2 (7.6)
SF-36 Mental Component Score	47.7 (11.1)	50.4 (8.2)	46.9 (13.7)
Overall Depression, Anxiety & Stress Scale (DASS) Score	27.1 (30.2)	18.3 (16.3)	15.4 (20.0)

Table 5: Comparison of quality of life outcomes between the three trial arms. SD – standard deviation; *LMAS – laryngeal mask airway supreme; SF-36 - Short Form-36. The SF-36 ranges from 0 (worst health) to 100 (best health). The DASS ranges from 0 (best health) to 42 (worst health). Seven patients declined to participate in this part of the study, and one patient with a pre-existing neurological deficit was excluded. One further patient was excluded from this analysis because they were unable to complete the assessment.*

Legends for Figures

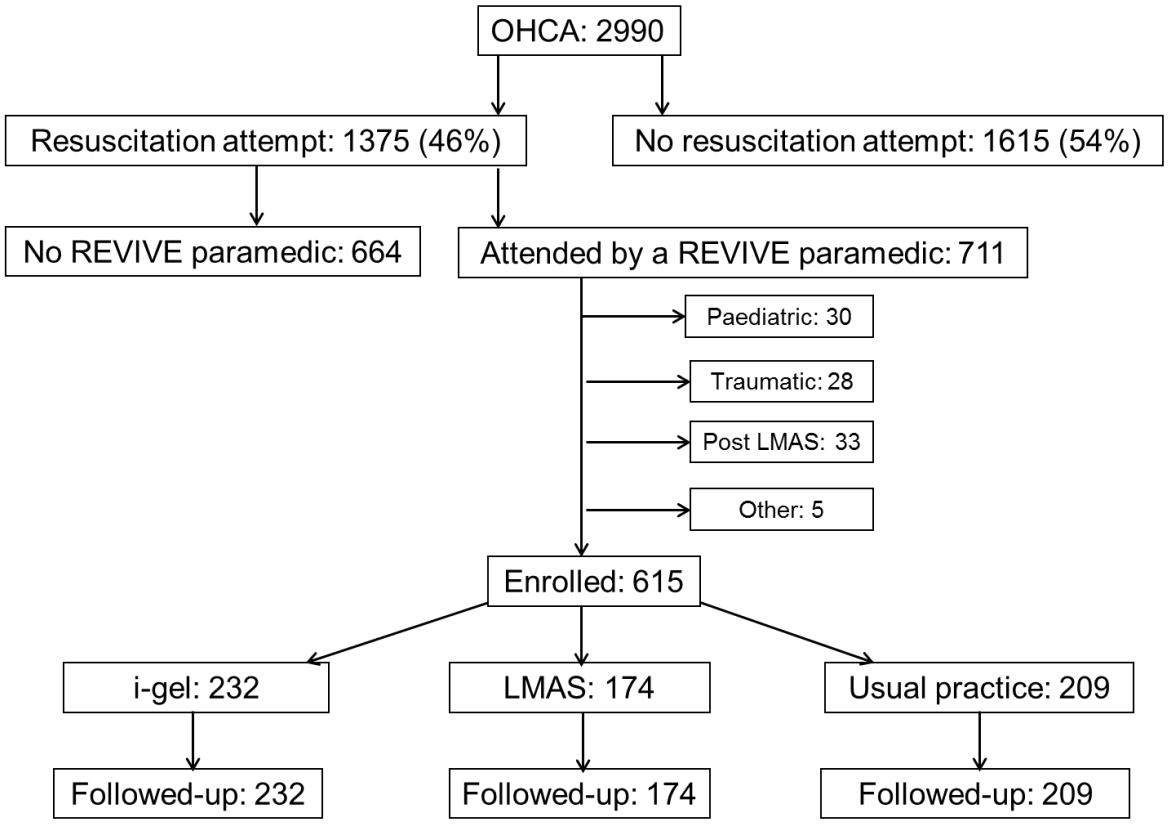

Figure 1: CONSORT Diagram. "Other" exclusions were: detained by Her Majesty's Prison Service (2 patients); mouth-opening < 2 cm (2 patients); previously recruited to the same study (1 patient). Post LMAS (33 patients) refers to those patients who were attended by a paramedic randomised to the LMAS arm after that arm was suspended (see text).