Supplementary Online Content

Benger JR, Kirby K, Black S, et al. Effect of a strategy of a supraglottic airway device vs tracheal intubation during out-of-hospital cardiac arrest on functional outcome: the AIRWAYS-2 randomized clinical trial. *JAMA*. doi:10.1001/jama.2018.11597

This supplementary material has been provided by the authors to give readers additional information about their work.

eText

Further information relating to Figure 1

The reasons given for paramedic withdrawal by tracheal intubation vs supraglottic airway device group were: (1) 70 (36 vs 34, respectively) had left the trust, service, or changed role; 13 (7 vs 6) did not want to follow the algorithm; 4 (2 vs 2) repeatedly failed to follow protocol; 6 were due to pregnancy or maternity leave (all randomized to tracheal intubation); 3 (1 vs 2) expressed that there was not enough time; 2 died (both randomized to supraglottic airway device); 7 (2 vs 5) gave no reason; and 8 (4 vs 4) provided other reasons. Of these 113 paramedics, 98 treated patients with an out-of-hospital cardiac arrest (49 tracheal intubation vs 49 supraglottic airway device) prior to withdrawal and 83 of these enrolled at least 1 eligible patient (40 vs 43, respectively). These trial patients were retained and included in the analysis.

The median number of patients with out-of-hospital cardiac arrest treated by a paramedic who later withdrew is 7 for tracheal intubation (interquartile range [IQR], 3-12; range, 1-54) and 6 for supraglottic airway device (IQR, 4-11; range, 1-31). The median number of trial patients treated by a paramedic who later withdrew is 3 for tracheal intubation (IQR, 1.0-5.5; range, 1-10) and 2 for supraglottic airway device (IQR,1-4; range, 1-12). Fewer patients allocated to tracheal intubation received advanced airway management (3419/4404 [77.6%] vs 4161 of 4883 [85.2%] randomized to the supraglottic airway device).

Further information relating to Figure 2

There were 41 patients (17 in the tracheal intubation group and 24 in the supraglottic airway device group) with missing return of spontaneous circulation status. Of these, 39 of 41 patients (15 for tracheal intubation vs 24 for supraglottic airway device) had a Modified Rankin Scale score in the 4 to 6 range (there were 37 deaths: 14 vs 23, respectively).

There were 9 patients (6 for tracheal intubation vs 3 for supraglottic airway device) with missing airway management details and all died.

72 patients in the TI group (2.1%) received a non-trial SGA only, all of whom had an mRS score of 4-6 (71 deaths). Out of these 72 patients, 2 had ROSC on arrival.

36 patients in the trial SGA group (0.9%) received a non-trial SGA only, all of whom had an mRS score of 4-6 (35 deaths). Out of these 36 patients, none had ROSC on arrival.

eTable 1. Patient demography and cardiac arrest details of trial patients, by allocated intervention and use of airway management

	Trial population				No advanced airway management[1]				Advanced airway management[1]			
All trial patients	**Randomised to TI (n=4,410)**		**Randomised to Trial SGA (n=4,886)**		**Randomised to TI (n=985)**		**Randomised to Trial SGA (n=722)**		**Randomised to TI (n=3,419)**		**Randomised to Trial SGA (n=4,161)**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age (median, IQR)	74	(62, 83)	73	(61, 82)	73	(60, 83)	71	(60, 82)	74	(63, 83)	73	(62, 82)
Male gender	2791/4410	63.3%	3132/4886	64.1%	615/985	62.4%	472/722	65.4%	2174/3419	63.6%	2658/4161	63.9%
999 call to first crew arrival time (mins; median, IQR)	8	(5, 11)	7	(5, 11)	8	(5, 11)	7	(5, 11)	8	(5, 11)	7	(5, 11)
Presenting rhythm												
Asystole	2356/4316	54.6%	2597/4791	54.2%	453/937	48.3%	348/681	51.1%	1901/3375	56.3%	2248/4108	54.7%
VF	979/4316	22.7%	1094/4791	22.8%	297/937	31.7%	226/681	33.2%	681/3375	20.2%	868/4108	21.1%
Pulseless VT	44/4316	1.0%	39/4791	0.8%	18/937	1.9%	11/681	1.6%	26/3375	0.8%	28/4108	0.7%
PEA	937/4316	21.7%	1061/4791	22.1%	169/937	18.0%	96/681	14.1%	767/3375	22.7%	964/4108	23.5%
Event witnessed	2788/4407	63.3%	3101/4883	63.5%	641/983	65.2%	490/719	68.2%	2144/3419	62.7%	2608/4161	62.7%
By bystander	2231/2788	80.0%	2493/3100	80.4%	472/641	73.6%	355/489	72.6%	1757/2144	81.9%	2135/2608	81.9%
By paramedic	557/2788	20.0%	607/3100	19.6%	169/641	26.4%	134/489	27.4%	387/2144	18.1%	473/2608	18.1%
Bystander CPR	2774/4406	63.0%	3149/4883	64.5%	567/983	57.7%	437/720	60.7%	2204/3418	64.5%	2709/4160	65.1%

TI=Tracheal Intubation, SGA=Supraglottic Airway Device, IQR=Interquartile Range, *VF=Ventricular Fibrillation, VT=Ventricular Tachycardia, PEA=Pulseless Electrical Activity, CPR=Cardiopulmonary Resuscitation*

Missing data (randomised to TI, randomised to SGA): [1]9 patients (6,3).

All patients are grouped by the allocation of the first study paramedic on scene.

eTable 2. Patient demography and cardiac arrest details of trial patients who received at least one advanced airway management attempt, by first intervention received

Trial patients with at least one advanced airway management attempt	Received TI first (n=2,840/9,296, 30.6%)		Received Trial SGA first (n=4,632/9,296, 49.8%)	
	n	%	n	%
Age (median, IQR)	74	(63, 83)	73	(61, 82)
Male gender	1780/2840	62.7%	2975/4632	64.2%
999 call to first crew arrival time (mins; median, IQR)	8	(5, 11)	7	(5, 11)
Presenting rhythm				
Asystole	1594/2806	56.8%	2509/4571	54.9%
VF	555/2806	19.8%	966/4571	21.1%
Pulseless VT	19/2806	0.7%	34/4571	0.7%
PEA	638/2806	22.7%	1062/4571	23.2%
Event witnessed	1782/2840	62.7%	2904/4632	62.7%
By bystander	1483/1782	83.2%	2353/2904	81.0%
By paramedic	299/1782	16.8%	551/2904	19.0%
Bystander CPR	1836/2839	64.7%	2998/4631	64.7%

TI=Tracheal Intubation, SGA=Supraglottic Airway device, IQR=Interquartile Range, VF=Ventricular Fibrillation, VT=Ventricular Tachycardia, PEA=Pulseless Electrical Activity, CPR=Cardiopulmonary resuscitation.
Patients are grouped by the treatment they received

eTable 3. Protocol deviations

All trial patients	Randomised to TI (n=4,410)		Randomised to Trial SGA (n=4,886)		Overall (n=9,296)	
	n	%	n	%	n	%
Wrong paramedic enrolled patient	4/4403	0.1%	8/4881	0.2%	12/9284	0.1%
Resulted in randomised allocation crossover	3/4	75.0%	4/8	50.0%	7/12	58.3%
Enrolling paramedic did not perform any airway management but another paramedic did	217/4405	4.9%	176/4883	3.6%	393/9288	4.2%
Trial patients with at least one advanced airway management attempt performed by enrolling paramedic	**Randomised to TI (n=3,419)**		**Randomised to Trial SGA (n=4,161)**		**Overall (n=7,580)**	
	n	**%**	**n**	**%**	**n**	**%**
Enrolling paramedic did not perform allocated intervention on first advanced airway attempt	316/3419	9.2%	149/4161	3.6%	465/7580	6.1%

TI=Tracheal Intubation, SGA=Supraglottic Airway device
Note:
All patients are grouped by the allocation of the first study paramedic on scene.
Further to those listed above, there were also 506 patients (190 TI, 316 SGA) for whom the enrolling paramedic made only one attempt at the allocated intervention.

eTable 4. Sensitivity analyses for primary outcome (modified Rankin Scale (mRS) score at discharge or 30 days)

Sensitivity analysis 1: Trial patients plus patients attended by a Trial paramedic but not resuscitated[1]	**Randomised to TI (n=10,744)**		**Randomised to Trial SGA (n=11,466)**		**Odds Ratio estimate (95% CI)**	**p-value**	**ICC**	**Risk difference estimate (95% CI)**	**p-value**
	n	**%**	**n**	**%**					
mRS (0 to 3; good recovery)	300/10741	2.79%	311/11462	2.71%	0.96 (0.81, 1.14)	0.63	0.06	-0.002 (-0.006, 0.003)	0.45
Sensitivity analysis 2: Trial patients who received at least one AAM[1]	**Randomised to TI (n=4,410)**		**Randomised to Trial SGA (n=4,886)**		**Odds ratio estimate (95% CI)**	**p-value**	**ICC**	**Risk difference estimate (95% CI)**	**p-value**
	n	**%**	**n**	**%**					
mRS (0 to 3; good recovery)	88/3418	2.6%	163/4158	3.9%	1.57 (1.18, 2.07)	0.002	0.10	0.014 (0.005, 0.022)	0.001
Sensitivity analysis 3: Trial patients who received at least one AAM[2]	**Received TI first (n=2,840)**		**Received Trial SGA first (n=4,632)**		**Odds ratio estimate (95% CI)**	**p-value**	**ICC**	**Risk difference estimate (95% CI)**	**p-value**
	n	**%**	**n**	**%**					
mRS (0 to 3; good recovery)	58/2838	2.0%	193/4630	4.17%	2.06 (1.51, 2.81)	<0.001	0.10	0.021 (0.012, 0.029)	<0.001

TI=Tracheal Intubation, SGA=Supraglottic Airway Device, CI=Confidence Interval, ICC=Intraclass Correlation Coefficient, AAM=advanced airway management.

Note:

[1] Patients are grouped by the allocation of the first study paramedic on scene.

[2] Patients are grouped by the first trial treatment they received. This only includes patients who have received at least one attempt at TI or trial SGA.

Odds ratios and risk differences are adjusted for stratification factors fitted as fixed effects. Odds ratios were obtained from a mixed effects logistic regression model with study paramedic fitted as a random effect. Risk differences were obtained by fitting a generalised linear model (binomial family and identity link) with standard errors adjusted for clustering. Wald p-values are displayed.

eTable 5. Additional secondary outcomes

Trial patients	Randomised to TI (n=4,410)		Randomised to Trial SGA (n=4,886)		Odds ratio estimate (95% CI)	p-value	ICC	Risk difference estimate (95%CI)	p-value
	n	%	n	%					
Actual sequence of airway interventions delivered (first two management attempts)									
OPA (1 attempt)	248/3686	6.7%	150/4321	3.5%					
OPA (2 attempts)	2/3686	0.1%	2/4321	0.1%					
OPA, then NPA	17/3686	0.5%	6/4321	0.1%					
OPA, then trial SGA	145/3686	3.9%	833/4321	19.3%					
OPA, then TI	1115/3686	30.3%	35/4321	0.8%					
OPA, then other SGA	42/3686	1.1%	21/4321	0.5%					
NPA (1 attempt)	10/3686	0.3%	8/4321	0.2%					
NPA, then OPA	2/3686	0.1%	2/4321	0.1%					
NPA, then trial SGA	4/3686	0.1%	19/4321	0.4%					
NPA, then TI	7/3686	0.2%	0/4321	0.0%					
NPA, then other SGA	1/3686	0.0%	0/4321	0.0%					
Trial SGA (1 attempt)	213/3686	5.8%	2388/4321	55.3%					
Trial SGA, then OPA	12/3686	0.3%	28/4321	0.7%					
Trial SGA, then NPA	0/3686	0.0%	4/4321	0.1%					
Trial SGA (2 attempts)	19/3686	0.5%	505/4321	11.7%					
Trial SGA, then TI	227/3686	6.2%	223/4321	5.2%					
Trial SGA, then Other SGA	0/3686	0.0%	1/4321	0.0%					
TI (1 attempt)	1092/3686	29.6%	64/4321	1.5%					
TI, then OPA	7/3686	0.2%	0/4321	0.0%					
TI, then NPA	1/3686	0.0%	0/4321	0.0%					
TI, then Trial SGA	79/3686	2.1%	9/4321	0.2%					
TI (2 attempts)	392/3686	10.6%	8/4321	0.2%					
TI, then Other SGA	24/3686	0.7%	0/4321	0.0%					
Other SGA (1 attempt)	20/3686	0.5%	14/4321	0.3%					
Other SGA, then TI	4/3686	0.1%	1/4321	0.0%					
Other SGA (2 attempts)	3/3686	0.1%	0/4321	0.0%					

Trial patients	Randomised to TI (n=4,410)		Randomised to Trial SGA (n=4,886)		Odds ratio estimate (95% CI)	p-value	ICC	Risk difference estimate (95%CI)	p-value
	n	%	n	%					
Any ventilation success with AAM	4086/4401	92.8%	4634/4874	95.1%					
TI	2163/3050	70.9%	573/753	76.1%					
Trial SGA	990/1112	89.0%	3465/4011	86.4%					
Other SGA	171/216	79.2%	33/44	75.0%					
Any ROSC during/after AAM by trial paramedic*	992/3416	29.0%	1295/4155	31.2%	1.13 (1.01, 1.27)	0.03	0.04	0.025 (0.001, 0.048)	0.04
Any ROSC during/after airway management by trial paramedic*	1139/3685	30.9%	1379/4318	31.9%					
AAM in place when patient first had ROSC*									
TI	689/1029	67.0%	165/1323	12.5%					
Trial SGA	241/1029	23.4%	1092/1323	82.5%					
Other SGA	29/1029	2.8%	12/1323	0.9%					
Other	70/1029	6.8%	54/1323	4.1%					
Final airway management in place in those who died on scene[1]									
TI	1322/1990	66.4%	364/2261	16.1%					
Trial SGA	501/1990	25.2%	1829/2261	80.9%					
Other SGA	114/1990	5.7%	17/2261	0.8%					
Other	53/1990	2.7%	51/2261	2.3%					
Final airway management in place in those who were admitted to ED[2]									
TI	1008/1429	70.5%	272/1899	14.3%					
Trial SGA	316/1429	22.1%	1558/1899	82.0%					
Other SGA	72/1429	5.0%	18/1899	0.9%					
Other	33/1429	2.3%	51/1899	2.7%					
Admitted to ED/hospital	1922/4410	43.6%	2263/4886	46.3%					
Survived to ED discharge	861/1919	44.9%	1033/2259	45.7%					
INTENSIVE CARE UNIT (ICU) STAY (patients survived to ED discharge only)	**(n=861)**		**(n=1033)**						
Admitted to ICU from ED	690/860	80.2%	869/1031	84.3%					

Trial patients	Randomised to TI (n=4,410)		Randomised to Trial SGA (n=4,886)		Odds ratio estimate (95% CI)	p-value	ICC	Risk difference estimate (95%CI)	p-value
	n	%	n	%					
Survived to ICU discharge	321/690	46.5%	366/869	42.1%					
Duration of initial ICU stay in patients who survived to ICU discharge (hours; median, IQR)	96.6	(45.7, 169.6)	100.5	(50.3, 197.5)					
Duration of ICU stay in patients who died in ICU (hours; median, IQR)	47.4	(18.0, 98.0)	47.0	(17.2, 97.9)					
HOSPITAL STAY (patients admitted to ED only)	**(n=1922)**		**(n=2263)**						
Survived to hospital discharge	372/1919	19.4%	392/2259	17.4%					
Duration of hospital stay in patients who survived to discharge (days; median, IQR)[3]	12.3	(6.9, 20.3)	14.0	(8.0, 23.8)					
Duration of hospital stay in patients who died before discharge (hours; median, IQR)[4]	1.7	(0.3, 20.4)	2.0	(0.4, 26.8)					
For all trial patients:									
Time from OHCA to time mRS was assessed (days) (median, IQR)[5]	25	(10, 68)	28	(10, 74)					

TI=Tracheal Intubation, SGA=Supraglottic Airway device, CI=Confidence Interval, ICC=Intraclass Correlation Coefficient, OPA= Oropharyngeal Airway, NPA= Nasopharyngeal Airway, AAM=advanced airway management, ROSC=Return of Spontaneous Circulation, ED=Emergency Department, IQR=Interquartile Range.

Missing data (randomised to TI, randomised to trial SGA): [1]1 patient (0, 1). [2]1 patient (1, 0). [3]310 patients (147, 163). [4] 31 patients (16,15). [5] 8275 patients (3919, 4356).

Note:

Odds ratios and risk differences are adjusted for stratification factors fitted as fixed effects. Odds ratios were obtained from a mixed effects logistic regression model with study paramedic fitted as a random effect. Risk differences were obtained by fitting a generalised linear model (binomial family and identity link) with standard errors adjusted for clustering. Wald p-values are displayed.

Odds ratios (from logistic regression) and risk differences are adjusted for EMS provider organisation (4 levels), paramedic experience (2 levels) and distance from the paramedic's base ambulance station to the usual destination hospital (2 levels). Risk differences were obtained by fitting a generalised linear model with the Binomial family and identity link. The odds ratios take into account the clustering of paramedics. The Wald p-values are displayed.

***** *Trial patients with at least one AAM attempt only*

All patients are grouped by the allocation of the first study paramedic on scene.

eTable 6. Compression fraction (used in two ambulance trusts for a subset of patients)

Trial patients enrolled during the period that compression fraction data were collected	Randomised to TI (n=32)			Randomised to Trial SGA (n=34)				
	n	Median	IQR	n	Median	IQR	Estimate (95% CI)	p-value
Compression Fraction[1]	32	83	(74, 89)	34	86	(81, 91)	GMR=0.82[2] (0.62, 1.07)	0.14

TI=Tracheal Intubation, SGA=Supraglottic Airway Device, IQR=Interquartile Range, CI=Confidence Interval, GMR=geometric mean ratio.

Note:

[1]*1239 (608 TI, 631 study SGA) eligible patients were attended by study paramedics with compression fraction cards. Of these, 108 cards (49 TI, 59 study SGA) were returned. Out of the 108 cards returned, 25 cards (8 TI, 17 study SGA) were unreadable, 16 (8 TI, 8 study SGA) contained no data and 1 card (1 TI, 0 study SGA) could not be used due to a mismatch in dates.*

[2] *Compression fraction was transformed due to skewness. The log of 100 minus compression fraction was fitted to a normal distribution.*

Geometric mean ratio is adjusted for stratification factors fitted as fixed effects with standard errors adjusted for clustering. Wald p-values are displayed.

All patients are grouped by the allocation of the first study paramedic on scene.

eTable 7. Risk ratios for the primary and secondary outcomes and the sensitivity analyses

All trial patients	Randomised to TI (n=4,410) n	%	Randomised to Trial SGA (n=4,886) n	%	Risk ratio (95% CI)	p-value
PRIMARY OUTCOME [1]						
mRS (0 to 3; good recovery)	300/4407	6.8%	311/4882	6.4%	0.92 (0.79, 1.08)	0.32
SECONDARY OUTCOMES [1]						
72 hour survival	575/4395	13.1%	664/4872	13.6%	1.04 (0.93, 1.15)	0.53
Initial ventilation success (up to two attempts at AAM)	3473/4397	79.0%	4255/4868	87.4%	1.11 (1.08, 1.13)	<0.001
Any loss of previously established airway	153/3081	5.0%	412/3900	10.6%	2.17 (1.79, 2.63)	<0.001
Regurgitation	1072/4372	24.5%	1268/4865	26.1%	1.06 (0.98, 1.15)	0.15
Aspiration	647/4337	14.9%	729/4824	15.1%	1.01 (0.90, 1.13)	0.85
Any ROSC during/after AAM by trial paramedic	992/3416	29.0%	1295/4155	31.2%	1.08 (1.00, 1.17)	0.04
ROSC on ED/hospital Admission	1249/4404	28.4%	1495/4880	30.6%	1.08 (1.01, 1.16)	0.02
SENSITIVITY ANALYSES						
Sensitivity analysis 1: Including all patients attended by a trial paramedic but not resuscitated[1]	**Randomised to TI (n=10,744) n**	**%**	**Randomised to Trial SGA (n=11,466) n**	**%**	**Risk ratio (95% CI)**	**p-value**
mRS (0 to 3; good recovery)	300/10741	2.79%	311/11462	2.71%	0.96 (0.81, 1.13)	0.64
Sensitivity analysis 2: Received at least one AAM[1]	**Randomised to TI (n=4,410) n**	**%**	**Randomised to Trial SGA (n=4,886) n**	**%**	**Risk ratio (95% CI)**	**p-value**

All trial patients	Randomised to TI (n=4,410)		Randomised to Trial SGA (n=4,886)		Risk ratio (95% CI)	p-value
	n	%	n	%		
mRS (0 to 3; good recovery)	88/3418	2.6%	163/4158	3.9%	1.54 (1.18, 2.01)	0.002
Sensitivity analysis 3: Received at least one AAM[2]	**Received TI first (n=2,840)**		**Received Trial SGA First (n=4,632)**		**Risk ratio (95% CI)**	**p-value**
	n	**%**	**n**	**%**		
mRS (0 to 3; good recovery)	58/2838	2.0%	193/4630	4.17%	2.00 (1.48, 2.70)	<0.001

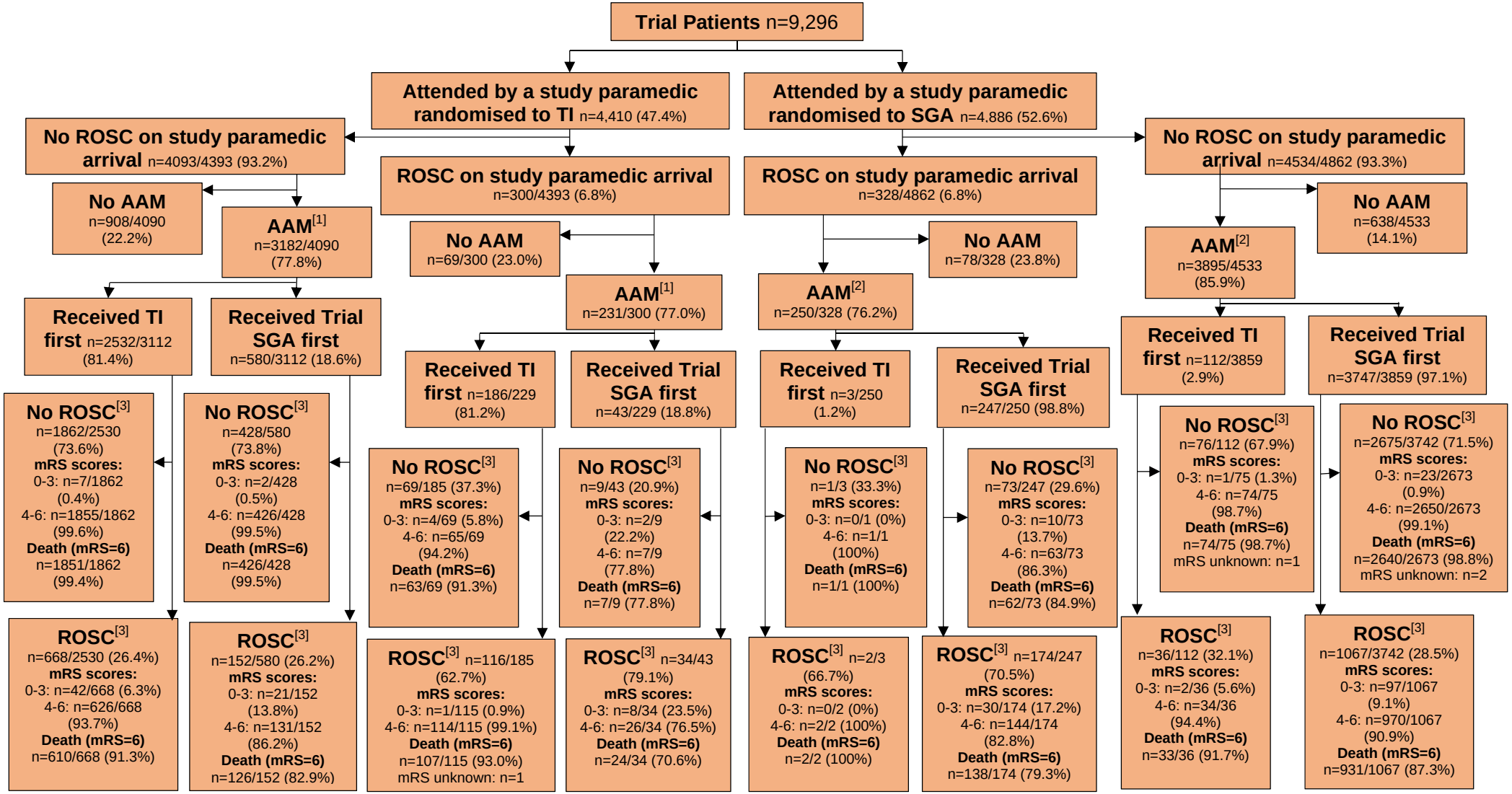
TI=Tracheal Intubation, SGA=Supraglottic Airway device, CI=Confidence Interval, mRS=modified Rankin Scale score, AAM=advanced airway management, ROSC=Return of spontaneous circulation, ED=Emergency department.

Note:

[1] Patients are grouped by the allocation of the first study paramedic on scene.

[2] Patients are grouped by the first trial treatment they received. This only includes patients who have received at least one attempt at TI or trial SGA.

Risk ratios are adjusted for stratification factors fitted as fixed effects. Risk ratios were obtained by fitting a generalised linear model (poisson family and log link) with standard errors adjusted for clustering. Wald p-values are displayed.

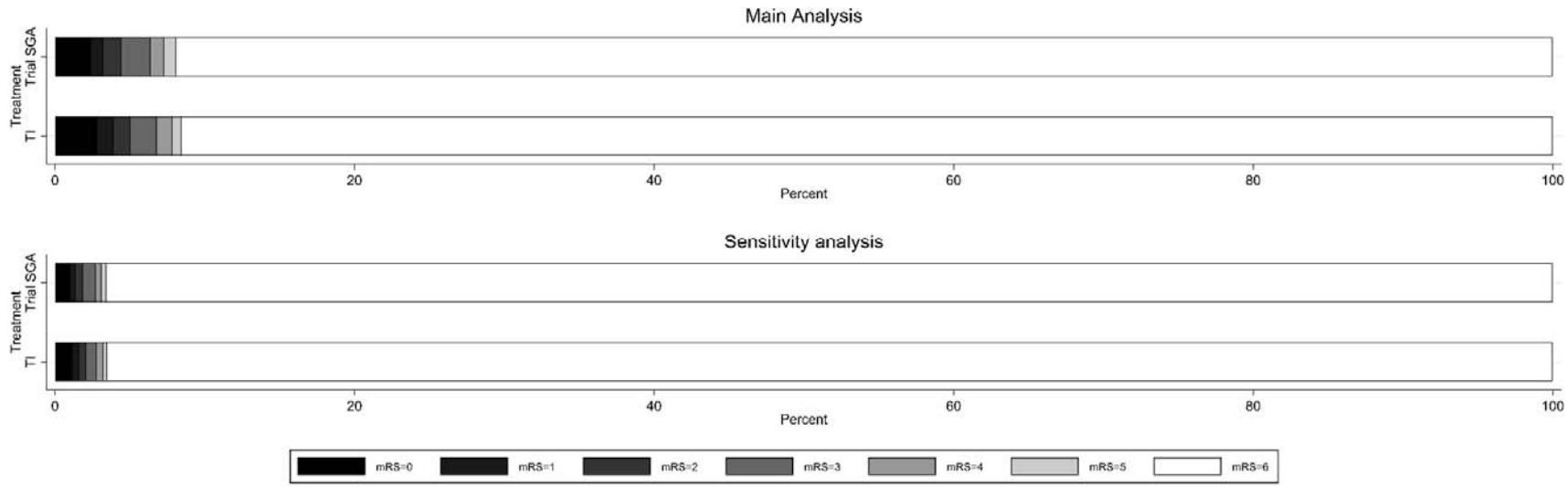


See notes overleaf

eFigure 1: Interventions received and patient outcome by study allocation extended

TI=Tracheal Intubation, SGA=Supraglottic Airway device, ROSC=Return of Spontaneous Circulation, mRS=Modified Ranking Score, AAM=Advanced Airway Management.
[1] 72 patients in the TI group (2.1%) received a non-trial SGA only, all of whom had an mRS score of 4-6 (71 deaths). Out of these 72 patients, 18 had ROSC during/after AAM
[2] 36 patients in the trial SGA group (0.9%) received a non-trial SGA only, all of whom had an mRS score of 4-6 (35 deaths). Out of these 36 patients, 12 had ROSC during/after AAM.
[3] ROSC here represents ROSC during or after AAM.
Note: 41 patients (17 TI, 24 Trial SGA) were missing ROSC on arrival details, 39 (15 TI, 24 Trial SGA) of whom had an mRS score of 4-6 (14 TI and 23 Trial SGA deaths). There were 4 patients (3 TI, 1 Trial SGA) missing AAM details, all of whom died. There were 8 patients (3 TI, 5 Trial SGA) who were missing ROSC during/after AAM details, 7 (2 TI, 5 Trial SGA) of whom had an mRS score of 4-6 (2 TI and 4 Trial SGA deaths)

eFigure 2. Breakdown of mRS scores for the main and sensitivity analyses



mRS=modified Rankin Score, SGA=supraglottic airway device, TI=tracheal intubation.
Notes:
Patients are grouped by the allocation of the first study paramedic on scene
eFigure 2 displays the breakdown of mRS scores relating to the analyses displayed in Figure 1. The sensitivity analysis includes all trial patients plus patients attended by a study paramedic who were not resuscitated.