Expedited transfer to a cardiac arrest centre for non-ST-elevation out-of-hospital cardiac arrest (ARREST): a UK prospective, multicentre, parallel, randomised clinical trial

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Summary

Background The International Liaison Committee on Resuscitation has called for a randomised trial of delivery to a cardiac arrest centre. We aimed to assess whether expedited delivery to a cardiac arrest centre compared with current standard of care following resuscitated cardiac arrest reduces deaths.

Methods ARREST is a prospective, parallel, multicentre, open-label, randomised superiority trial. Patients (aged ≥18 years) with return of spontaneous circulation following out-of-hospital cardiac arrest without ST elevation were randomly assigned (1:1) at the scene of their cardiac arrest by London Ambulance Service staff using a secure online randomisation system to expedited delivery to the cardiac catheter laboratory at one of seven cardiac arrest centres or standard of care with delivery to the geographically closest emergency department at one of 32 hospitals in London, UK. Masking of the ambulance staff who delivered the interventions and those reporting treatment outcomes in hospital was not possible. The primary outcome was all-cause mortality at 30 days, analysed in the intention-to-treat (ITT) population excluding those with unknown mortality status. Safety outcomes were analysed in the ITT population. The trial was prospectively registered with the International Standard Randomised Controlled Trials Registry, 96585404.

Findings Between Jan 15, 2018, and Dec 1, 2022, 862 patients were enrolled, of whom 431 (50%) were randomly assigned to a cardiac arrest centre and 431 (50%) to standard care. 20 participants withdrew from the cardiac arrest centre group and 19 from the standard care group, due to lack of consent or unknown mortality status, leaving 411 participants in the cardiac arrest centre group and 412 in the standard care group for the primary analysis. Of 822 participants for whom data were available, 560 (68%) were male and 262 (32%) were female. The primary endpoint of 30-day mortality occurred in 258 (63%) of 411 participants in the cardiac arrest centre group and in 258 (63%) of 412 in the standard care group (unadjusted risk ratio for survival 1·00, 95% CI 0·90–1·11; p=0·96). Eight (2%) of 414 patients in the cardiac arrest centre group and three (1%) of 413 in the standard care group had serious adverse events, none of which were deemed related to the trial intervention.

Interpretation In adult patients without ST elevation, transfer to a cardiac arrest centre following resuscitated cardiac arrest in the community did not reduce deaths.

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See Comment page 1300

*Collaborators are listed in the appendix pp 3–7

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Introduction

There are marked regional variations in survival following resuscitated out-of-hospital cardiac arrest (OHCA), which are attributable to resources, personnel, and infrastructure in addition to patient characteristics.[1–3] Regionalisation of care improves outcomes in patients with time-critical illness by concentrating services within centres, increasing the number of patients treated and therefore the skills and experience of health-care providers within those centres.[4] Implementing prehospital systems of care for OHCA management would work in a similar manner to networks for ST-elevation myocardial infarction, with ambulance staff providing prompt identification and delivery of patients to a designated cardiac arrest centre.[5,6] Post-arrest care with early interventions for ischaemia-reperfusion injury and treatment of the underlying cause has preferential outcomes.[7] This care might be better delivered in a cardiac arrest centre; however, observational studies yield conflicting results due to confounding variables, including selection bias and heterogeneity of care.[8] As a result, the International Liaison Committee on Resuscitation highlighted the need for a randomised trial.

FN MOTOL

ARREST TRIAL

JIŘÍ KARÁSEK

European Heart Journal (2015) **36**, 2793–2867
doi:10.1093/eurheartj/ehv316

ESC GUIDELINES

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care☆

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It is recommended that post-resuscitation care is performed in high-volume expert centres capable of offering multidisciplinary intensive care treatment, including primary coronary interventions, electrophysiology, cardiac assist devices, cardiac and vascular surgery and therapeutic hypothermia.	I	B	245, 246
The creation of regional networks for the treatment of cardiac arrest should be considered to improve outcomes.	IIa	B	245

Cardiac arrest centres

No specific recommendation

Adult patients with non-traumatic OHCA should be considered for transport to a cardiac arrest centre according to local protocol.

An expert consensus paper published by several European organisations including the Association of Acute Cardiovascular Care (ACVA) of the European Society of Cardiology (ESC), the ERC and the ESICM, states that the minimum requirements for a cardiac arrest centre are 24/7 availability of an on-site coronary angiography laboratory, an emergency department, an ICU, imaging facilities, such as echocardiography, CT, and MRI.[16] Based on evidence from a systematic review, ILCOR suggests that wherever possible, adult patients with non-traumatic OHCA cardiac arrest should be cared for in cardiac arrest centres.[17]

European Heart Journal (2017) 38, 1645–1652
doi:10.1093/eurheartj/ehx104

CLINICAL RESEARCH
Acute coronary syndromes

Distance to invasive heart centre, performance of acute coronary angiography, and angioplasty and associated outcome in out-of-hospital cardiac arrest: a nationwide study

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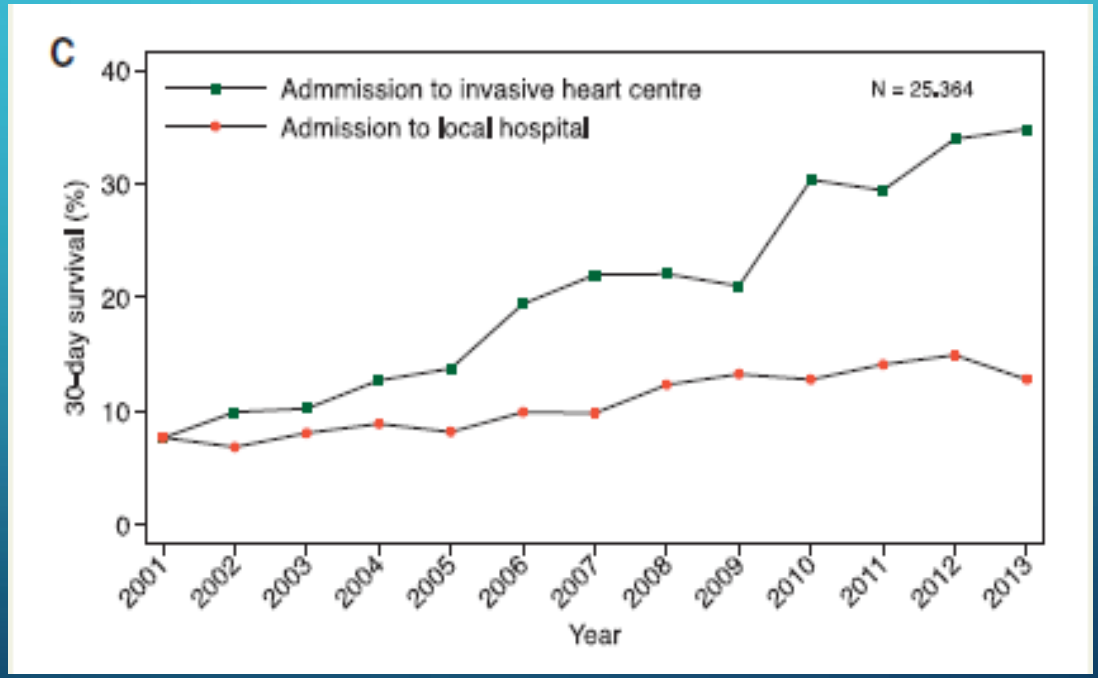


Figure 2. Adjusted Odds of Survival to Charge and to 30 Days

Study or subgroup	log[Odds ratio]	SE	OR (95% CI)	Weight, %
Survival to discharge				
Balian et al,[17] 2019	0.36	0.14	1.43 (1.08-1.89)	10.5
Callaway et al,[18] 2010	0.09	0.16	1.10 (0.80-1.50)	10.2
Cha et al,[19] 2012	1.01	0.13	2.74 (2.12-3.54)	10.8
Chocron et al,[20] 2017	0.24	0.35	1.27 (0.64-2.51)	6.3
Couper et al,[21] 2018	0.03	0.18	1.03 (0.72-1.47)	9.7
Cudnik et al,[22] 2012	-0.03	0.15	0.97 (0.73-1.29)	10.5
Shin et al,[29] 2011	0.59	0.12	1.81 (1.43-2.30)	11.0
Stub et al,[30] 2011	0.02	0.19	1.02 (0.70-1.48)	9.5
von Vopelius-Feldt et al,[31] 2021	0.34	0.11	1.41 (1.14-1.75)	11.2
Subtotal (95% CI)			1.36 (1.08-1.73)	89.7
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 44.62$, $df = 8$ ($P < .001$); $I^2 = 82\%$				
Test for overall effect: $z = 2.57$ ($P = .01$)				
Survival to 30 d				
Kashiura et al,[23] 2020	-0.27	0.15	0.76 (0.56-1.03)	10.3
Subtotal (95% CI)			0.76 (0.56-1.03)	10.3
Heterogeneity: Not applicable				
Test for overall effect: $z = 1.79$ ($P = .07$)				
Total (95% CI)			1.28 (1.00-1.64)	100.0
Heterogeneity: $\tau^2 = 0.13$; $\chi^2 = 60.62$, $df = 9$ ($P < .001$); $I^2 = 85\%$				
Test for overall effect: $z = 1.97$ ($P = .05$)				
Test for subgroup differences: $\chi^2 = 9.00$, $df = 1$ ($P = .003$); $I^2 = 88.9\%$				

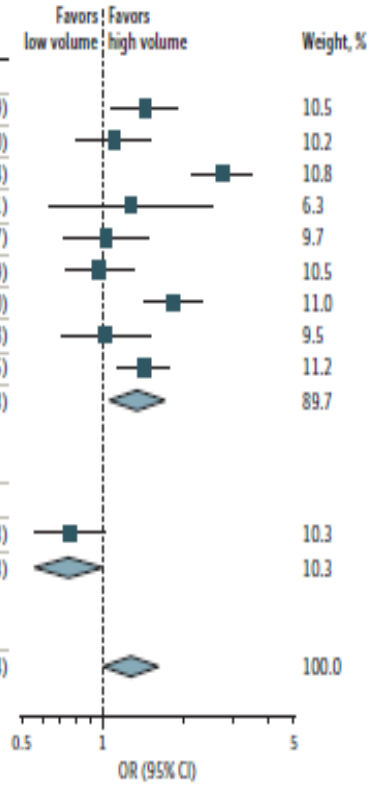
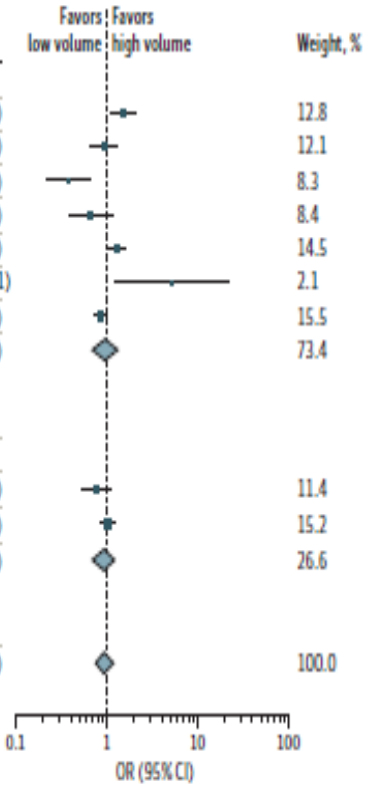


Figure 3. Adjusted Odds of Good Neurological Outcomes at Discharge and 30 Days

Study or subgroup	log[Odds ratio]	SE	OR (95% CI)	Weight, %
Good neurological outcomes at discharge				
Balian et al,[17] 2019	0.41	0.15	1.51 (1.11-2.05)	12.8
Couper et al,[21] 2018	-0.06	0.17	0.94 (0.67-1.32)	12.1
Cudnik et al,[22] 2012	-0.97	0.28	0.38 (0.22-0.66)	8.3
Lee et al,[25] 2015	-0.41	0.28	0.66 (0.39-1.14)	8.4
Mumma et al,[26] 2015	0.28	0.11	1.32 (1.06-1.64)	14.5
Schober et al,[28] 2016	1.65	0.74	5.20 (1.22-22.11)	2.1
Worthington et al,[32] 2017	-0.14	0.08	0.87 (0.74-1.02)	15.5
Subtotal (95% CI)			0.98 (0.71-1.33)	73.4
Heterogeneity: $\tau^2 = 0.12$; $\chi^2 = 35.35$, $df = 6$ ($P < .001$); $I^2 = 83\%$				
Test for overall effect: $z = 0.16$ ($P = .88$)				
Good neurological outcomes at 30 d				
Kashiura et al,[23] 2020	-0.26	0.19	0.77 (0.53-1.12)	11.4
Matsuyama et al,[25] 2017	0.03	0.09	1.03 (0.87-1.22)	15.2
Subtotal (95% CI)			0.94 (0.72-1.22)	26.6
Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 1.91$, $df = 1$ ($P = .17$); $I^2 = 48\%$				
Test for overall effect: $z = 0.49$ ($P = .63$)				
Total (95% CI)			0.96 (0.77-1.20)	100.0
Heterogeneity: $\tau^2 = 0.08$; $\chi^2 = 37.35$, $df = 8$ ($P < .001$); $I^2 = 79\%$				
Test for overall effect: $z = 0.37$ ($P = .71$)				
Test for subgroup differences: $\chi^2 = 0.04$, $df = 1$ ($P = .84$); $I^2 = 0\%$				



JAMA Network Open

Original Investigation | Emergency Medicine

Association of High-Volume Centers With Survival Outcomes Among Patients With Nontraumatic Out-of-Hospital Cardiac Arrest
A Systematic Review and Meta-Analysis

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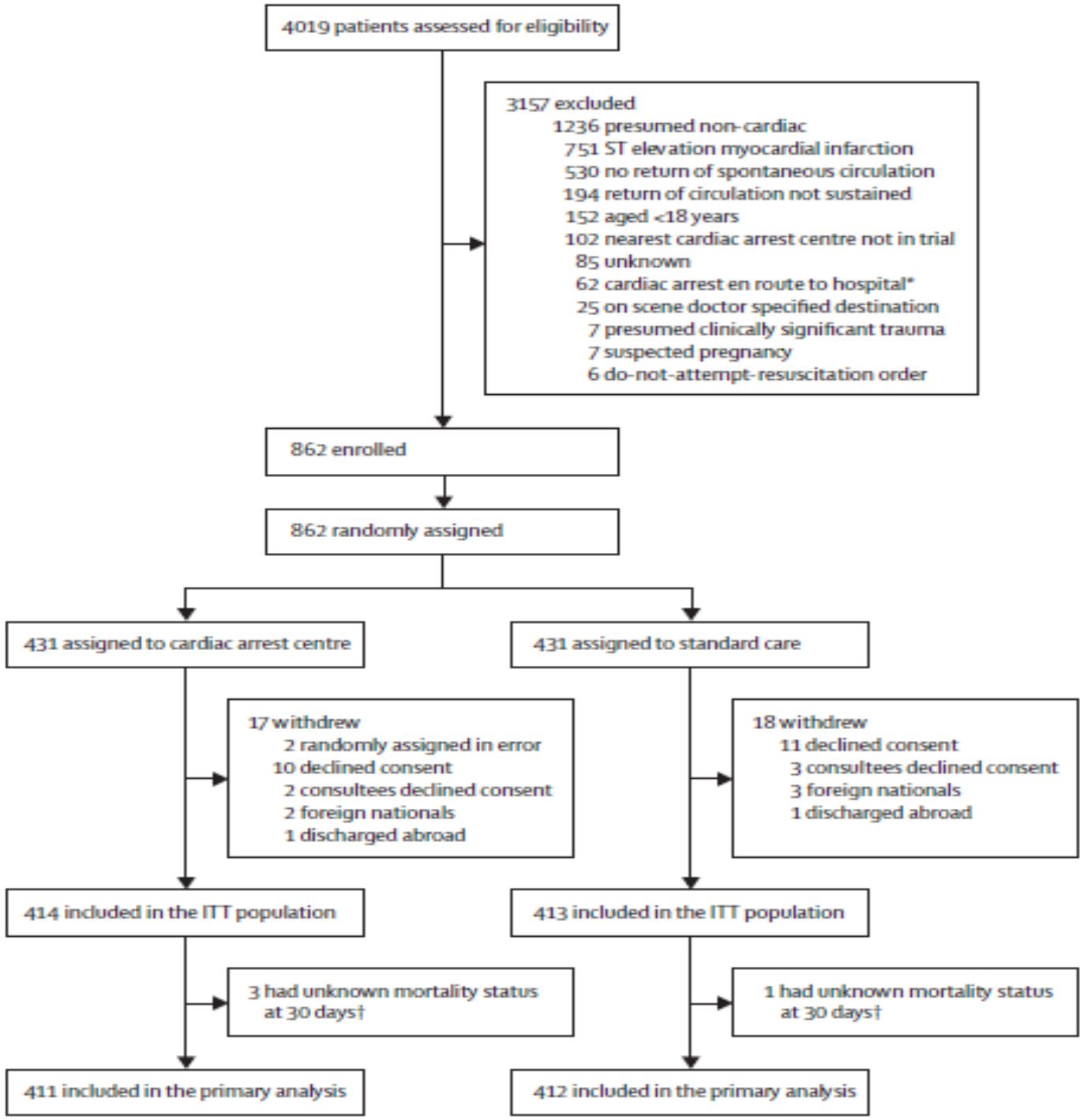
- Multicentrická otevřená, randomizovaná studie
- (2018-2022), přerušená pro COVID
- Inclusion: věk nad 18, ROSC, předpokládaná kard. zástava, EKG bez ST elevací
- Exclusion: těhotenství, předpokládaná nekard. etiologie, ST elevace na EKG po KPR
- Randomizace 1:1 (7x cathlab CAC vs. 32 ED nejbližší nemocnice)

- Primární endpoint: 30- denní mortalita
- Sekundární endpointy: 3-měsíční mortalita, neurolog. status při dimisi a 3.měsíc


Watford General
Barnet
North Middlesex
Harrsfield
Whipps Cross
King George
Northwick Park
Whittington
Queen's
Homerton
Royal Free
Hillingdon
Hammersmith
UCH
Barts
Royal London
Newham
St Mary's
Ealing
Chelsea & Westminster
St Thomas'
West Middlesex
Char X
King's College
Queen Elizabeth
Lewisham
Darent Valley
St George's
Kingston
Croydon University
St Heller
Princess Royal
Epsom



	Cardiac arrest centre group (n=414)	Standard care group (n=413)
Age, years	63·8 (16)	63·2 (16)
Sex		
Male	285/412 (69%)	275/410 (67%)
Female	127/412 (31%)	135/410 (33%)
Ethnicity		
White	224/414 (54%)	224/413 (54%)
Asian	69/414 (17%)	69/413 (17%)
Afro-Caribbean	21/414 (5%)	25/413 (6%)
Other	39/414 (9%)	45/413 (11%)
Not known	61/414 (15%)	50/413 (12%)
Medical history		
Diabetes	98/385 (26%)	90/376 (24%)
Hypertension	182/376 (48%)	190/372 (51%)
Smoking status		
Never smoked	96/414 (23%)	83/413 (20%)
Ex-smoker	50/414 (12%)	53/413 (13%)
Current smoker	41/414 (10%)	55/413 (13%)
Not known	227/414 (55%)	222/413 (54%)
Hypercholesterolaemia	99/342 (29%)	83/315 (26%)
Peripheral vascular disease	12/360 (3%)	13/348 (4%)
Cerebrovascular disease	26/369 (7%)	39/362 (11%)
Chronic renal failure	33/375 (9%)	31/362 (9%)
Known ischaemic heart disease	83/362 (23%)	63/353 (18%)
Previous myocardial infarction	54/364 (15%)	48/362 (13%)
Previous percutaneous coronary intervention	46/362 (13%)	34/349 (10%)
Family history of heart disease	32/179 (18%)	32/168 (19%)
Preceding symptoms before cardiac arrest	122/267 (46%)	142/260 (55%)
Chest pain	29/122 (24%)	43/142 (30%)
Dizziness	11/122 (9%)	29/142 (20%)
Breathlessness	50/122 (41%)	49/142 (35%)
Palpitations	2/122 (2%)	8/142 (6%)
Other symptoms	61/122 (50%)	74/142 (52%)

Data are mean (SD) or n/N (%). Ethnicity and smoking status had "Not known" as a response category in the case report form and so the denominator for these variables is the total number of patients in the intention-to-treat population; other variables did not have this option, and therefore the denominator for all other variables is the number of patients for whom data were available.

Table 1: **Baseline characteristics of the intention-to-treat population**

	Cardiac arrest centre group (n=414)	Standard care group (n=413)
Location of arrest		
Private	208 (50%)	242 (59%)
Public	206 (50%)	171 (41%)
Witnessed arrest		
Bystander	308 (74%)	307 (74%)
LAS	30 (7%)	25 (6%)
Not witnessed	76 (18%)	81 (20%)
Presenting cardiac rhythm		
AED non-shockable, asystole, or PEA	184 (44%)	188 (46%)
AED shockable, VF, or pulseless VT	229 (55%)	225 (55%)
Not known	1 (<1%)	0
Initial CPR attempt		
Bystander	290 (70%)	313 (76%)
LAS	123 (30%)	100 (24%)
Not performed	1 (<1%)	0
Time from arrest to LAS CPR start, min	9 (7–12); n=278	10 (7–12); n=275
First defibrillation performed		
Public access defibrillator	49 (12%)	54 (13%)
LAS	211 (51%)	198 (48%)
Not performed	142 (34%)	150 (36%)
Not known	12 (3%)	11 (3%)
Time from arrest to first defibrillation, min	10 (7–14); n=194	11 (7–14); n=199
Number of shocks delivered	2 (1–4); n=242	2 (1–3); n=226
Adrenaline administered	267 (65%)	260 (63%)
Adrenaline dose, mg	2 (1–4); n=260	2 (1–4); n=254
Amiodarone administered	68 (16%)	58 (14%)
Amiodarone dose, mg	300 (300–300); n=65	300 (300–300); n=52
Mechanical CPR	100/412 (24%)	93/411 (23%)
Time from arrest to ROSC, mins	24 (15–33); n=310	25 (16–34); n=314
Field termination of resuscitation	2 (1%)	3 (1%)
Time from arrest to hospital arrival, min	84 (68–104); n=332	77 (63–96); n=328
Post-ROSC electrocardiogram*		
ST-segment elevation	7 (2%)	5 (1%)
Bundle branch block	116 (28%)	99 (24%)
ST-segment depression or T wave changes (or both)	156 (38%)	181 (44%)
No acute changes	91 (22%)	83 (20%)
No electrocardiogram	44 (11%)	45 (11%)

Data are n (%), median (IQR), or n/N (%). The number of participants for whom data were obtained is presented after median values and n values when the number was less than the total intention-to-teat population. AED=automated external defibrillator. CPR=cardiopulmonary resuscitation. LAS=London Ambulance Service. PEA=pulseless electrical activity. ROSC=return of spontaneous circulation. VF=ventricular fibrillation. VT=ventricular tachycardia.
* The electrocardiogram was reviewed independently after trial enrolment and randomisation. Defibrillation data were analysed for patients with shockable rhythm only.

Table 2: **Prehospital key events in the intention-to-treat population**

arrest is provided in the appendix (pp 33–34). A cardiac cause of arrest was identified in 260 (63%) of 414 patients in the cardiac arrest centre group and 245 (59%) of 413 patients in the standard care group. In patients with a

vs 93 [23%] of 406). A higher proportion of patients in the cardiac arrest centre group than in the standard care group were admitted to intensive care (330 [80%] of 414 *vs* 286 [69%] of 413), received haemodynamic support (297 [72%] of 412 *vs* 252 [62%] of 406), ventilatory support (353 [86%] of 412 *vs* 312 [76%] of 410), and renal support (46 [11%] of 411 *vs* 34 [8%] of 403). A higher proportion of patients in the cardiac arrest centre group than in the standard care group had coronary angiography (231 [56%] of 412 *vs* 153 [37%] of 410). The median time to

London Ambulance Service cardiac arrest annual audit data, resuscitation is attempted in approximately 36% of all out-of-hospital cardiac arrests. Resuscitation can be withheld if

	Cardiac arrest centre group (n=414)	Standard care group (n=413)	RR, OR, or mean difference (95% CI)	Adjusted OR* (95% CI) or p value	Risk difference (95% CI)
Primary endpoint					
30-day mortality	258/411 (63%)	258/412 (63%)	RR 1·00 (0·90 to 1·11)	1·09 (0·73 to 1·63)	0·2% (−6·5 to 6·8)
Secondary endpoints					
3-month mortality	267/411 (65%)	263/411 (64%)	RR 1·02 (0·92 to 1·12)	--	1·0% (−5·6 to 7·5%)
mRS score at discharge			OR 1·00 (0·76 to 1·32)	0·99	--
0	70/413 (17%)	78/402 (19%)	--	--	--
1	23/413 (6%)	31/402 (8%)	--	--	--
2	22/413 (5%)	12/402 (3%)	--	--	--
3	15/413 (4%)	9/402 (2%)	--	--	--
4	10/413 (2%)	2/402 (1%)	--	--	--
5	16/413 (4%)	12/402 (3%)	--	--	--
6	257/413 (62%)	258/402 (64%)	--	--	--
mRS score at 3 months			OR 0·98 (0·73 to 1·31)	0·87	--
0	75/399 (19)	69/390 (18%)	--	--	--
1	22/399 (6%)	32/390 (8%)	--	--	--
2	17/399 (4%)	9/390 (2%)	--	--	--
3	5/399 (1%)	9/390 (2%)	--	--	--
4	9/399 (2%)	3/390 (1%)	--	--	--
5	4/399 (1%)	5/390 (1%)	--	--	--
6	267/399 (67%)	263/390 (67%)	--	--	--
mRS score at discharge					
Favourable	130/413 (32%)	130/402 (32%)	RR 1·01 (0·92 to 1·11)	0·79	0·9% (−5·5 to 7·3)
Unfavourable	283/413 (69%)	272/402 (68%)	--	--	--
mRS score at 3 months					
Favourable	119/399 (30%)	119/390 (31%)	RR 1·01 (0·92 to 1·11)	0·83	0·7% (−5·7 to 7·1)
Unfavourable	280/399 (70%)	271/390 (70%)	--	--	--
Mean EQ-5D-5L score	0·68 (0·32); n=97†	0·72 (0·25); n=92†	Mean difference −0·04 (−0·12 to 0·05)	--	--

Data are n/N (%) and mean (SD), unless otherwise specified. Mortality refers to all-cause mortality. mRS=modified Rankin Scale. OR=odds ratio. RR=risk ratio. *Adjusted OR calculated due to convergence issues. †The number of participants for whom data were obtained.

Table 3: **Primary and secondary outcomes**

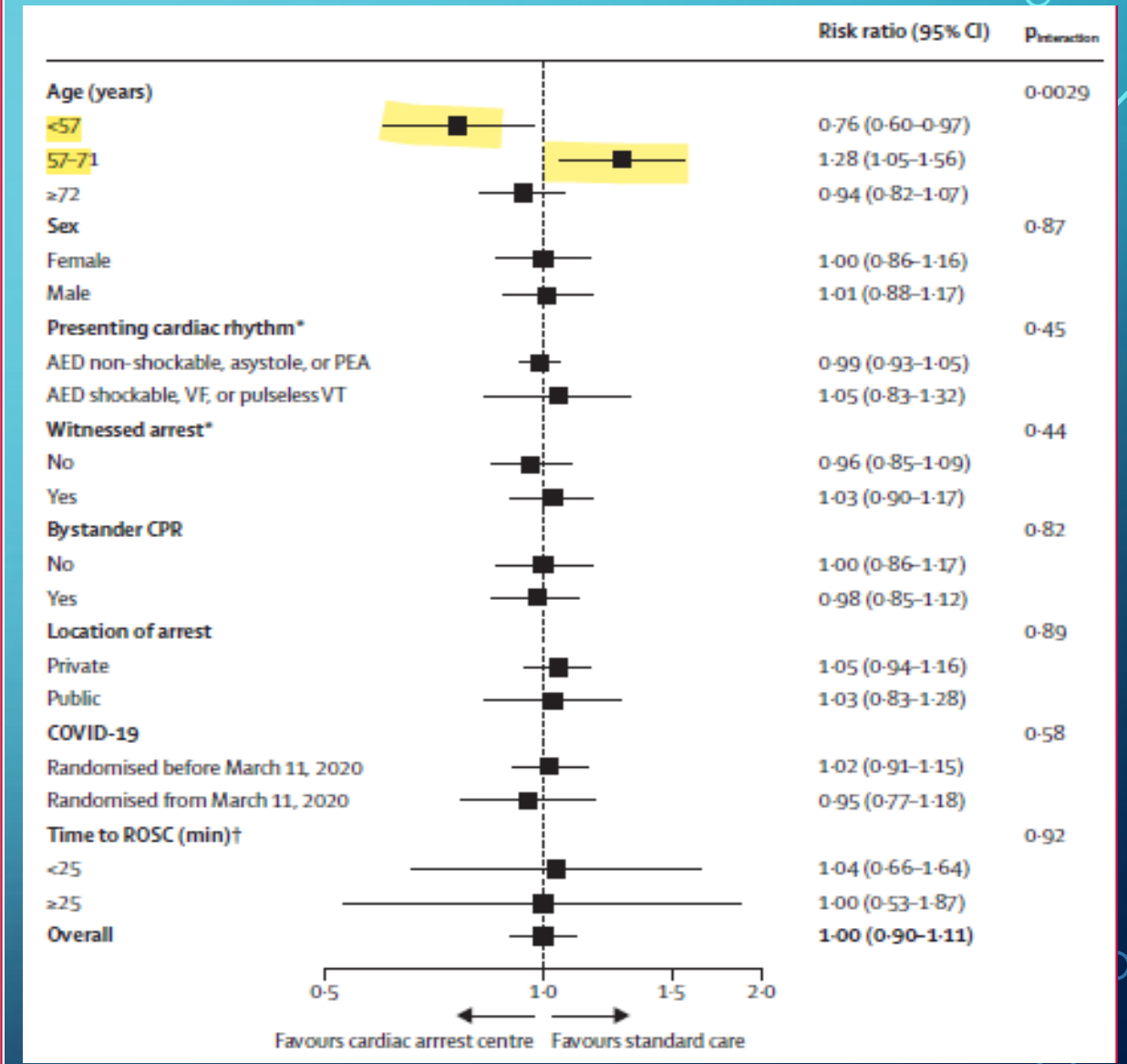


Table 3: Out-of-hospital cardiac arrest volume and survival in London per centre (2017-18).

Cardiac Arrest Centre	Number of patients	Survival
	Median 125 (IQR 100 to 167)	Mean 45.7% (±0.1)
St Thomas Hospital	112	47.8% (32/67)
Barts Heart Centre	125	55.8% (53/95)
King's College Hospital	189	36.5% (46/126)
Harefield Hospital	61	54.2% (26/48)
St George's Hospital	184	36.4% (47/129)
Royal Free Hospital	150	42.5% (45/106)
Hammersmith Hospital	88	47% (31/66)
Non-CAC	Number of patients	Survival
	Median 62 (IQR 44 to 79)	Mean 14.4% (±0.1)
Barnet Hospital	50	26.1% (6/23)
Northwick Park Hospital	110	9.6% (5/52)
Hillingdon Hospital	68	15.8% (6/38)
Queens Hospital, Romford	119	9.6% (5/52)
University College Hospital	34	26.7% (4/15)
Homerton Hospital	44	4.8% (1/21)
Ealing Hospital	56	16.7% (5/30)
Queen Elizabeth Hospital	107	15.9% (7/44)
North Middlesex Hospital	107	17.3% (9/52)
West Middlesex Hospital	78	9.4% (3/32)
Whittington Hospital	32	18.8% (3/16)
Kingston Hospital	64	16.1% (5/31)
University Hospital Lewisham	58	17.2% (5/29)
St Helier Hospital	44	10% (2/20)
Newham Hospital	80	10.3% (3/29)
St Mary's Hospital	70	25.7% (9/35)
King George Hospital	57	4.8% (1/21)
Charing Cross Hospital	34	9.1% (1/11)
Chelsea & Westminster Hospital	33	27.8% (5/18)
Princess Royal Hospital	59	3.1% (1/32)
Croydon University Hospital	69	14.7% (5/34)
Darent Valley Hospital	11	0% (0/4)
Watford Hospital	Unavailable	Unavailable
Royal London Hospital	86	18.4% (7/38)
Whipps Cross Hospital	76	16.7% (5/30)
Central Middlesex Hospital	Unavailable	Unavailable
Chase Farm Hospital	Unavailable	Unavailable
East Surrey Hospital	Unavailable	Unavailable

ZÁVĚR

- Není rozdíl v 30 denním přežívání při umístění pacienta po OHCA s ROSC bez ST elevací do cardiac arrest centra vs. nejbližší nemocnice
- Rovněž není rozdíl v 3 měsíčním přežívání a dobrém neurologickém výsledku
- Pacienti přijímaní do CAC jsou více přijímáni na JIP, vyžadují více oběh., ventil. podporu a RRT bez vlivu na mortalitu a mají více koronarografií
- V subanalýze pacienti maldší 57 let profitují stran mortality více z CAC, ve věku 57-71 let z lok. nemocnice