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Feasibility of data linkage in the PARAMEDIC Trial: a cluster randomised trial of mechanical chest compression in out of hospital cardiac arrest

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4	2		compression in out of hospital cardiac arrest.	
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- 1 Word count
- 2 Abstract: 287
- 3 Main body: 3525 (excluding Tables/Figures/titles/notes/legends)

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2	1	Abstroat
5 4	T	Abstract
5	2	Objectives: There is considerable interest in reducing the cost of clinical trials. Linkage of trial data to
6	3	administrative datasets and disease-specific registries may improve trial efficiency, but has not been
7	1	reported in resuscitation trials conducted in the LIK. To assess the feasibility of utilising national
8		administrative and clinical datasets to follow up notionts transported to bespital following
9	5	auministrative and cinical datasets to follow up patients transported to hospital following
10	6	attempted resuscitation in a cluster randomised trial of a mechanical chest compression device in
11 12	7	out of hospital cardiac arrest (OHCA).
12	8	Methods: Hospital data on trial participants were requested from Hospital Episode Statistics (HES):
14	0	the Intensive Care National Audit and Pessarch Centre (ICNAPC): and Myesardial Ischaemia National
15	10	Audit Desiget (MINAD) and National Audit of Deseutes and Constants Intervention (NADCI), using
16	10	Audit Project (MINAP) and National Audit of Percutaneous Coronary Intervention (NAPCI), using
17	11	unique patient identifiers. Linked data were received between June 2014 and June 2015.
18	12	Results: Of 4471 patients randomised in the PARAMEDIC trial, 2398 (53.6%) were not known to be
19 20	13	deceased at emergency department arrival and were eligible for linkage. We achieved an overall
21	1/	match rate of 86.7% in the combined HES A&F innational and Critical care dataset with variable
22	15	match rate of 00.7% in the combined HES Add, inpatient and entited care dataset, with variable
23	15	match rates (4.2-80.4%) in multiduda datasets. No strong evidence of substantial blas was found in
24	16	patient demographics, cardiac arrest related characteristics and major outcomes between HES
25	17	matched and unmatched groups, in the linkage apart from location, response time and ROSC at
26	18	handover.
27	10	Constructions. This should show that it is for either the two should be the form the sure housing boots in a
28	19	conclusions: This study shows that it is reasible to track patients from the pre-hospital setting
29	20	through to hospital admission using routinely available administrative datasets with a moderate to
31	21	high degree of success. This approach has the potential to complement the trial data with the
32	22	demographic and clinical management information about the studied cohort, as well as to improve
33	23	the efficiency and reduce the costs of follow-up in cardiac arrest trials.
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1 Strengths and limitations of this study

- First study evaluating the supplement of routinely collected administrative data in a cardiac arrest trial in the UK.
- Data linkage was made to different UK national registries.
- The matching reliability was suboptimal due to relaxed matching criteria, matching method and possible data quality issues.
- Routine data were not fully available for all trial patients transported to hospital.
- The findings of our study are not generalisable to facilitate trial recruitment since it was • considered unrealistic in the clinical context of cardiac arrest. to occurrence on the second

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1 Background

Well conducted and reported randomised controlled trials (RCTs) are considered the gold standard in evaluation of new or established clinical interventions. In cardiac arrest resuscitation science, only a small minority (1%) of contemporary international guideline recommendations are based on the highest level of evidence from more than one RCT, meta-analysis of high quality RCTs, or RCTs corroborated by high quality registry studies.¹ High quality trials to address outcomes of interest to patients following cardiac arrest (e.g. long term survival, neurocognitive status and disability)² are complex, labour intensive and expensive to perform. Many studies in cardiac arrest are therefore too small or inadequately conducted (with a predominance of observational studies which are prone to bias) to provide reliable estimates of treatment effect or harm to patients. Consequently, for the majority of resuscitation interventions, there is a paucity of high quality evidence. Funders (typically government agencies) have called for proposals for low-cost, more efficient trials.³

Traditional trial methods of patient tracking and data access in individual hospitals is challenging with limited resources. Cardiovascular medicine has attempted to improve the efficiency of the trial design by pioneering the concept of registry-based randomised trials, using clinical quality registries and administrative datasets. In the Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction (TASTE) trial, undertaken in Sweden, both patient enrolment and follow up were conducted using the Swedish Web System for Enhancement and Development of Evidence-based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry.⁴ On publication, this registry-based trial was hailed as the 'next disruptive technology' in clinical research, and as a new clinical trial paradigm.^{5 6} Subsequent registry-based trials have been reported in a comparison of radial versus femoral access in women undergoing percutaneous coronary intervention in the United States,⁷ and of supplemental oxygen versus ambient air in patients with suspected acute myocardial infarction in Sweden.⁸

To our knowledge, however, there are no reports of registry-based randomised trials in resuscitation science. However, should accessing registry data to ascertain outcomes in a prehospital cardiac arrest trial (e.g. length of stay/patient pathways/survival status) to be feasible, this could be one way of significantly improving efficiency and reducing costs of conducting high quality randomised trials in resuscitation.

30 In the PARAMEDIC trial, the in-hospital data collection process was complex, expensive and labour 31 intensive, with research paramedics visiting multiple hospitals across large geographical areas to 32 extract data from hospital records. Patients transported to hospital following resuscitation from 33 cardiac arrest follow multiple clinical pathways depending on their clinical status and treatments. As

hospital data are routinely collected and managed by national registries, utilising these registries
 could save resources and time in the in-hospital data collection and potentially reduce the burden
 on patients and relatives in the sensitive period following cardiac arrest.

4 This paper reports our assessment of the feasibility of linking data collected for the purposes of 5 patient follow up in a pragmatic, cluster randomised controlled trial of a mechanical chest 6 compression device undertaken in the United Kingdom (UK) prehospital setting, with large national 7 administrative and specialist registries.

8 Methods

The PARAMEDIC trial examined the effectiveness of LUCAS-2, a mechanical chest compression device, in 4471 patients with out of hospital cardiac arrest (OHCA). The study was a cluster randomised trial whereby emergency medical service (EMS) vehicles were randomised to carry the LUCAS-2 device (intervention) or not (control). Full details of the trial protocol have been published previously.⁹ In summary, adults with OHCA where resuscitation was attempted by EMS personnel and attended by a trial vehicle were included. Patients with traumatic cardiac arrest or suspected to be pregnant were excluded. Trial recruitment ran from April 15, 2010 to June 10, 2013. We have previously reported primary outcome (30-day survival),¹⁰ secondary outcomes,¹¹ an economic analysis¹² and characteristics of patients who were not resuscitated.¹³

18 Data sources

The PARAMEDIC trial utilised four sources of data that were linked to the trial dataset: UK National Health Service (NHS) Hospital Episodes Statistics (HES), Myocardial Ischaemia National Audit Project (MINAP),¹⁴ National Audit of Percutaneous Coronary Interventions (NAPCI),¹⁵ and Case Mix Programme (CMP)¹⁶ to obtain data on hospital stay and treatment or procedures that trial patients received in hospital.

We used the MINAP, NAPCI and CMP data for the health economic analysis¹² and long-term post admission outcomes¹¹ and to validate the hospital length of stay or stay in the intensive care (secondary outcomes for the efficacy part of the trial), and also to gain insight into the specifics of the treatment or procedures that trial patients received during their hospital stay. Characteristics of the registries are summarised in Table 1.

29 Table 1: Characteristics of registries, participation and case ascertainment.

Registry/Dataset Source Description case ascertainme during the trial per	Registry/Dataset	Source	Description	Participation and case ascertainment during the trial peri
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Paramedic trial	Warwick Clinical Trials Unit	Trial patient cohort that survived admission to a hospital	n/a
Hospital Episode Statistics (HES)	NHS Digital (NHSD)	Collection of information on all NHS hospital inpatients, Accident and Emergency (A&E), critical care and outpatients which enables health care providers to be paid according to their levels of activity.	All hospitals Case ascertainment 100%
Case Mix Programme (CMP)	Intensive Care National Audit and Research Centre (ICNARC)	Audit of patient outcomes from all adult, general critical care units in England, Wales and Northern Ireland. Other specialist units, including neurosciences, cardiac and high dependency units, also participate	Over 90% of critical care units Case ascertainment not reported
Myocardial Ischaemia National Audit Project (MINAP)	National Institute for Cardiovascular Outcomes Research (NICOR)	National audit of patients with acute coronary syndrome admitted to all hospitals in England, Wales and Northern Ireland. Data are collected prospectively at each hospital by secure electronic system, electronically encrypted and transferred online to a central database	All hospitals Case ascertainment not reported
NAPCI (National Audit of Percutaneous Coronary Interventions)	National Institute for Cardiovascular Outcomes Research (NICOR)	National audit of all PCI procedures from NHS and non-NHS hospitals in the United Kingdom.	All hospitals Case ascertainment 97%

1 Note: *: Case ascertainment – Rate (e.g. %) of eligible cases included in a registry/database.

2 Patient population

3 Patients (denominator) for this linkage study were patients from the PARAMEDIC trial who were

4 transported to hospital by EMS and not known to be deceased (i.e. documented as alive or unknown

5 status) on arrival at the emergency department (ED).

6 Since NHS Digital, responsible for HES, only provides annual data up to 1st April each year, no data on

7 trial patients recruited on or after 1st April 2013 had any HES data returned for this data request. We

8 therefore limited our analysis of the linked registry data to patients recruited to the PARAMEDIC trial
9 between April 2010 and March 2013.

Study approvals

The PARAMEDIC trial was approved by the Coventry Research Ethics Committee (reference 09/H1210/69) and sponsored by the University of Warwick, UK. The study was conducted in accordance with the principles of Good Clinical Practice and the Mental Capacity Act (2005). Specific approval for access to personal data without consent and the data linkage reported in this paper was obtained from the Confidentiality Advisory Group, part of the Health Research Authority (reference:

1 ECC 2-02 (c)/2011). At the time of the study this activity was undertaken by the National Information

2 Governance Board for Health and Social Care Ethics and Confidentiality Committee.

3 Data linkage procedure

Data access applications were submitted to national administrative and disease registries between 2012-2014 to request patient case mix and clinical variables (Supplementary Table 1). The following patient identifiers were sent to the NHSD, ICNARC and NICOR to identify their clinical records: trial number, cardiac arrest date, ambulance service case number, 999 call time, hospital name, hospital arrival time, hospital handover time, patient name, NHS number, home address and postcode. The trial data were linked to the two NICOR datasets (MINAP and NAPCI) on two separate occasions by a different member of NICOR staff, which reassuringly generated the same results. Extracted anonymous data were encrypted and sent back to the trial team between June 2014 and June 2015.

Linked data may contain multiple, non-event related hospital records within the requested linkage period. We firstly used patient cardiac arrest (trial event) date to identify the records with exactly matched admission/visit date in the respective data sources. However, event and admission dates could be different due to potential data definition discrepancies. For instance, a trial event could occur before midnight and the patient was admitted to hospital after midnight. Therefore, we relaxed the date match criterion to a 5-day range (date of cardiac arrest with +/- 2 days). A matched record was redefined as if the admission/visit date falls in the range. We considered the range would be sufficiently large to mitigate against any date discrepancies in different sources and also be reasonably small to reduce the chance of mismatch in the case of early re-admission. Where multiple records could be matched to a single trial event in the same routine dataset, separate rules were used to extract the retrieved information: 1) where a patient had multiple episodes in HES, only the one with recorded death or discharge date was retained. If a patient had not been discharged from hospital, the episode with latest ward admission date was used. 2) Where multiple admissions to ICU were recorded in CMP, only the first ICU admission was linked to a trial event. 3) Since the MINAP dataset provided to us by NICOR only contained year and month of admission, only the earliest admission was used. 4) Only the first procedure was included for the linkage to the NAPCI registry data, since patients can have more than one interventional procedure (and thus another record) during the index admission.

30 Data linkage rate

For HES data, we developed the linkage and match rate for linked and matched (or correctly linked)cases as follows:

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3	1	HES linkage rate = N of patients with linked HES inpatient, Critical care or A&E data
4	2	N of patients not known to be deceased at ED
5	3	
7	4	HFS match rate = N of patients with matched (correctly linked) HFS inpatient. Critical care or A&E data
8	5	N of patients not known to be deceased at ED
9	6	
10	-	
11	7	Similar equations were used to determine the rates for each of the datasets i.e. MINAP, NAPCI and
12	8	CMP. As we were not able to confirm which patient should actually be collected in these datasets,
14 15	9	we employed same denominator used in the above equations.
16 17	10	Data linkaae ayality
18	11	Match rank is an indicator used in HES to show the confidence of match: 1 suggests the best match
19 20	12	and 8 the worst. Level 1-3 appear to be of high quality as cases are matched based on a combination
21	13	of unique NHS number and data of date of birth, sex and home postcode. The quality of linkage in
22	1/	matched HES was therefore summarised on the basis of percentage of level 1-3
23	14	matched HES was therefore summarised on the basis of percentage of level 1-5.
24 25	15	Data representativeness
26	16	Data representativeness was assessed in two comparisons. The first comparison intended to assess
27	17	
28	17	whether the patients with correctly linked (i.e. matched) HES data could be representative of the
30	18	trial population. It was carried out in patients with and without matched HES inpatient, Critical Care
31	19	or A&E data (comparison 1). The second comparison intended to assess the difference between two
32 33	20	critical care data sources. We were not able to compare data from these two sources directly as
34 25	21	some patient care data were collected in both databases. Hence, we split the patients by their linked
35 36	22	data sources and made the comparison between patients with HES Critical Care only, with CMP data
37 38	23	only and with both HES Critical Care and CMP data (comparison 2).
39 40	24	For both comparisons, we compared patient and event characteristics between the datasets.
41	25	Continuous variables were compared using Mann-Whitney test in comparison 1 and Kruskal-Wallis
42 43	26	test in comparison 2. Categorical variables were compared using Chi-square test. A two-sided p
44	27	value <0.05 was considered statistically significant. All analyses were conducted in SAS v9.3 (Cary,
45 46	28	NC, USA).
47		
48 40	29	Data security and destruction
50	30	We followed the Warwick Clinical Trials Unit Standard Operating Procedures (SOPs) for data storage,
51 52	31	transfer, and data sharing. The data were retained and destroyed in accordance with relevant
52 53 54	32	regulations and the University of Warwick's Data Sharing Agreements.
55	33	Results
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1	In the PARAMEDIC trial, 2695 patients were transported to hospital and not known to be deceased				
2	at ED. Of these 2398 (89.0%) were recruited between April 2010 and March 2013 and were				
3	therefore in	ncluded in this study (referred to as "I	inkage patients"). The c	lata requests to NHSD,
4	ICNARC and NICOR retrieved different numbers of patient clinical records.				
5	Summary o	f the linkage			
6	The flow ch	nart of the linkage to H	HES is shown in F	igure 1. The linkage pa	tients were grouped into
7	admitted (p	patients with matched	HES Critical car	e data) and not admitte	ed (patients with other
8	matched H	ES data). Meanwhile,	patients with ma	atched CMP data were	also summarised in the
9	flowchart. ⁻	This presented a com	oarison betweer	CMP and HES Critical (Care. 303 patients were
10	matched in	both CMP and HES C	ritical Care. Ove	rall. the linkage to HES (data achieved a match rat
11	of 86.7% (2	079 of 2398) with allo	wed variation ir	n dates (date of cardiac	arrest with +/- 2 davs).
12	slightly imp	proved from the use o	f exact date mat	ch approach (84.1%).	
	0,1				
13	Linkage qua	ality was high in matcl	hed cases: level	1-3 accounted for 97.99	%. In unmatched cases,
14	91.5% (292	of 319) had no linked	HES data and t	ne rest, while linked wit	h non-trial even related
15	data, had a good match rank (<=3).				
16	The summary of linkage and match rate in each dataset are shown in Table 2. All datasets contained				
17	multiple linked records, indicating some patients had been linked to multiple admissions with				
18	possible multiple episodes. Among the 2398 linkage patients, individual match rate varied dependin				
19	on the hospitalisation stage and received treatments. HES A&E had the highest individual match rat				
20	(80.4%). In the patients admitted to ICU, CMP provided 53 more matched patients with a lower				
21	proportion of unmatched data in linked patients compared to HES Critical Care.				
22					
23	Figure 1: Li	nkage match rate and	l flowchart of pa	tients retrieving HES or	CMP data.
24					
- 1					
25					
26	Table 2: Su	mmary of linked PARA	MEDIC trial pat	ients to the respective r	egistry databases
	Data		Number of	Number of linked	Number of matched
	source	Dataset	linked records	patients (linkage rate)*	patients (match rate)*
		HES Inpatient	12875	1617 (67.4%)	771 (32.2%)
	NHSD	HES Critical care	545	433 (18.1%)	354 (14.8%)
		HES A&E	6/3/	2186 (01 2%)	1927 (80.4%)

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	Overall	19854	2277 (95.0%)	2079 (86.7%)
ICNARC	СМР	435	410 (17.1%)	407 (17.0%)
NCAP	MINAP	244	218 (9.1%)	182 (7.6%)
	PCI	153	128 (5.3%)	101 (4.2%)

Note: *: Percentage is calculated using the number in the column divided by 2398 linkage patients.

A summary of retrieved information for each linked dataset as well as the degree of data missingness for each field is available in the online supplementary materials. In Supplementary Table 2, the trial patients that had not been matched to the HES records were similar to those that with matched records in age (mean age 71.8 and 73.6 respectively), male (67.4% and 63.3% respectively were male). They were also similar between groups in initial cardiac arrest aetiology where most were of cardiac origin (85.3% and 85.9% respectively) and in initial rhythm (shockable rhythm 31.0% and 31.3%). Patients with unmatched data were more likely to have had a cardiac arrest in a public place (27.9%) compared with of those with matched records (16%), witnessed by bystander (53.3% versus 46.3%) and had longer EMS response time (7.2 versus 6.1 minutes). Supplementary Table 3 illustrates the comparison of demographic and event characteristics of patients with matched HES Critical Care and CMP data. Characteristics were similar in all three groups, except for a significant difference in the EMS response time.

Discussion

This study aimed to demonstrate the feasibility of collecting trial outcome data during patient follow up in a prehospital cardiac arrest trial via linkage to national registries. We achieved an overall match rate of 86.7% in 2398 patients using HES data. The data linkage provided important administrative and additional clinical data that allowed extended analyses of the intervention effect and provided more details of patient journey in the trial. We also evaluated the representativeness of retrieved HES and CMP data by comparing patient and trial event characteristics. No substantial difference was found in patients with and without matched HES inpatient, Critical Care or A&E data, as well as in patients with matched HES Critical Care only, CMP only and both datasets.

This was the first study evaluating the supplement of routinely collected administrative data in a cardiac arrest trial in the UK. Our match rate was in line with observational studies linking EMS data to hospital records,¹⁷⁻²⁰ and data validation studies.²¹ Our experience suggests it is feasible to obtain relevant data from administrative databases in a cardiac arrest trial. In addition to the high match rate reported in this paper, the matched data are deemed to be sufficiently representative of the trial population. The comparison between patients with and without matched HES showed low level

1 of imbalance of event characteristics. Overall the results suggested no substantial bias. We have

2 found similar results in the matched ICU data.

The unmatched cases were likely to be associated with missing or inaccurate data. Data quality could be at increased risk due to the challenging circumstances of cardiac arrest and complexity of patient handling following hospital arrival. In addition, routine data in the chosen registries are not systematically adjudicated. Lack of clinical engagement may compromise the case ascertainment and data quality,²² leading to suboptimal linkage. NHS Digital employs deterministic and probabilistic methods in the data linkage. The latter calculates probability weight based on combinations of linkage variables and determines linkage based on a cut-off threshold. Although this method largely improves the linkage, it could incorrectly link record pairs and miss valid ones, undermining the reliability of linkage.

Linkage to individual routine datasets resulted in variable match rates. HES A&E generated the highest rate of 80.4% as most patients were taken by EMS to ED for assessment before being admitted to specialist hospital units. Other rates reflected the proportion of specific groups of patients in the linkage. The CMP, MINAP and NAPCI registries are focused on selected patients with a specific diagnosis and/or requiring specialist care, reflected in strict inclusion and exclusion criteria; for example MINAP comprises data on patients with suspected and/or confirmed acute coronary syndrome, NAPCI on interventional cardiology whilst CMP registry collects data on patients admitted to critical care/intensive care units within any given hospital. In this study, MINAP and NAPCI generated 9.1% and 5.3% respectively. Patients who die in the ED are less likely to be recorded on MINAP, and only those patients receiving interventional cardiology are recorded in NAPCI.

Use of routine data has the potential to reduce the costs of conducting trials. The cost of the TASTE trial was reported as US\$300,000, or approximately \$50 per patient,⁴ 2 per cent of the cost of a traditional randomised trial, but differs from the PARAMEDIC trial in that we did not use registry data to identify and recruit patients in the challenging and time-pressured setting of our-of-hospital cardiac arrest. In the West of Scotland Coronary Prevention (WOSCOPS) trial, data linkage reduced costs of long term follow up to less than one per cent of trial budget.²³ However, the time cost of linkage could be unrealistic for some trials. Linkage for the PARAMEDIC trial took up to three years from application to the trial team obtaining the data. It has been suggested that NHS Digital, who performed the linkage to HES for our study was overwhelmed with data linkage applications.²⁴ This may limit the usefulness of administrative data in trials with funder-imposed deadlines for completion.

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1 Limitations:

2 Our study had several limitations. The matching reliability was suboptimal due to relaxed matching 3 criteria (using range of event date), matching methods and potential issues of data quality and completeness, common to administrative data. Bohensky et al.²⁵ conducted an evidence synthesis of 4 data linkage studies and identified factors such as sub-optimal or incomplete linkage leading to 5 6 systematic bias. They considered the participant or population characteristics that can influence the 7 validity and completeness of data linkage and may in turn lead to systematic bias in reporting. They 8 reported variation in quality of data linkage across geographical/hospital sites, which could be due to 9 high staff turnover or not sufficient resources allocated to the data collection and/or coding. We 10 have not considered such variations in this study, but overall match quality was high in the matched 11 cases.

Secondly, routine data were not fully available for all patients transported to hospital. Some patients were not included in the linkage as their data were not available in HES at the time of our data application. Although no substantial bias was shown, the generalisability of results could be limited. Several data fields were incomplete, for example, MINAP captures most ST elevation myocardial infarction (STEMI) cases but data for non-STEMI are less complete. We also cannot confirm how many patients required specialist care and should be included in non-HES datasets. Therefore, we were unable to assess and report the impact of unmatched cases in in the linkage to these registries.

Thirdly, we used the first matched admission without considering repeated or later admissions. We
 were therefore unlikely to fully describe patients' hospital pathway based on matched information.

21 Fourthly, our focus for the present study was on assessing the feasibility of using administrative data

for purposes of follow-up. We did not assess the utility of administrative data to facilitate

recruitment of trial patients since this was considered unrealistic in the clinical context of cardiacarrest.

Fifthly, we did not assess the financial cost of manual data collection at hospitals to compare withthe cost of the use of registries in the trial linkage.

27 *Recommendations*

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Based on our experience, we made the following recommendations to improve the use of datalinkage in trials:

1. When planning a trial using linkage to administrative registries, careful planning is required to assess availability of the required data. Linkage to routine data in different jurisdictions or

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1	availability	
3	 Trialists need to be mindful of prolonged processes for regulatory approvals, data release 	
4	and validation. These processes may extend beyond trial funding.	
5	3. Data linkage is a lengthy often unpredictable process in the application stage, possibly due	
6	to the restricted capacity of registries funded primarily to assess quality of care. Most	
7	registries in the NHS are funded as national audits and do not have sufficient resources for	
8	the timely processing of data sharing requests.	
9	4. The quality of routinely collected data in the national registries may be inferior to that	
10	collected using traditional trial processes. Registry data are collected in high volume with	
11	limited resources and the validation process is unlikely to be as robust as in trials that are	
12	better resourced. Moreover, collected variables in registries are reviewed periodically and	
13	may change to reflect advances in clinical practice, which can impact on data completeness.	
14	5. It is common for registries to charge a fee for data release, which should be costed in to trial	
15	budgets.	
16	Conclusions	
17	This study shows that it is fassible to track patients from the are bespital setting through to bespital	
17 10	admission using routinely available administrative datasets with a mederate to high degree of	
10	success. This may improve the officiency and reduce the costs for longer term follow up in cardiac	
20	arrest trials	
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1 Declaration of interests

2 GDP, RL, TQ, CDD and SG report grants from NIHR HTA Programme during the conduct of the study.

3 The other authors declare no competing interests.

4 Author's contributions

CS, JH, SG and GDP led on the data linkage. CJ analysed data. CJ, TQ and LG drafted the manuscript
with input from the co-authors; RL, CS, JH, CDD, HP, MAS, NR, SJM, SG and GDP reviewed the
manuscript. All authors approved the final version.

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- 19 British Heart Foundation and Resuscitation Council (UK).
- 20 Data sharing statement

21 No additional data sharing available.

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Supplementary materials:

	HES Inpatient	All
CSK apparation	No	606 (79.6%)
CSK Operation	Yes	155 (20.4%)
	The usual place of residence, including no fixed abode	192 (24.9%)
	Temporary place of residence when usually resident elsewhere	4 (0.5%)
	Repatriation from high security psychiatric hospital (from 1999-2000)	0 (0.0%)
	Repatriation from high security psychiatric hospital (from 1999-2000)	0 (0.0%)
	Penal establishment - court (from 1999-2000)	0 (0.0%)
	Penal establishment - police station (from 1999-2000)	0 (0.0%)
	Penal establishment - court and police station excluded (from 1999-2000 to 2006-07)	0 (0.0%)
	High security psychiatric hospital, Scotland (from 1999-2000)	0 (0.0%)
	NHS other hospital provider - high security psychiatric accommodation	0 (0.0%)
	NHS other hospital provider - medium secure unit (from 1999- 2000)	32 (4.2%)
	NHS other hospital provider - ward for maternity patients or neonates	0 (0.0%)
Destination of	NHS other hospital provider - ward for patients who are mentally	
discharge	ill or have learning disabilities	0 (0.0%)
-	NHS run nursing home, residential care home or group home	3 (0.4%)
	Local authority Part 3 residential accommodation - where care is provided (from 1996-97)	0 (0.0%)
	Local authority foster care, but not in Part 3 residential accommodation - where care is provided (from 1996-97)	0 (0.0%)
	LA home or care (1989-90 to 1995-96)	0 (0.0%)
	Non-NHS run hospital - medium secure unit (from 2003-04)	1 (0.1%)
	Non-NHS (other than local authority) run residential care home (from 1996-97 to 2003-04) and care home (from 2003-04)	3 (0.4%)
	Non-NHS (other than local authority) run nursing home (from 1996-97 to 2003-04)	0 (0.0%)
	Non-NHS run hospital	0 (0.0%)
	Non-NHS (other than local authority) run hospice	2 (0.3%)
	Non-NHS institution (1989-90 to 1995-96)	0 (0.0%)
	Not applicable	7 (0.9%)
	Not known	1 (0.1%)
	Died	522 (67.7%)
Method of	Discharged on clinical advice or with clinical consent	234 (30.4%)
discharge	Self discharged, or discharged by a relative or advocate	5 (0.6%)

Supplementary Table 1: Summary of retrieved information in each linked dataset.

	Secretary or a court	0 (0.0%)
	Baby was still born	0 (0.0%)
	Not applicable: patient still in hospital	10 (1 3%)
	Not known: a validation error	0 (0 0%)
	Died	522 (67 79
	Missing	8/ (10 9%)
	Least deprived 10%	64 (8 2%)
	Less deprived 10-20%	12 (5.6%)
	Less deprived 20 20%	45 (5.0%)
	Less deprived 20.40%	47 (0.1%) 25 (4 5%)
IND 2001 index	Less deprived 40 50-40%	55 (4.5%)
IIVID 2004 IIIUEX	Less deprived 40-50%	50 (0.5%)
		80 (10.4%)
	More deprived 20-30%	84 (10.9%)
	More deprived 30-40%	58 (7.5%)
	More deprived 40-50%	61 (7.9%)
	Most deprived 10%	165 (21.49
Hospital length of	stay*	7.7 (20.3)
	HES A&E	All
	Emergency departments	1865 (96.8
A&F department	Consultant-led mono specialty accident and emergency service'	0 (0.0%)
type - A&E only	Other type of A&E. Excludes NHS walk-in centres	4 (0.2%)
-, ,	NHS walk-in centres	1 (0.1%)
	Not known	57 (3.0%)
	Admitted to hospital bed / became a lodged patient of the same	
	health care provider	560 (29.1%
	Discharged – follow-up treatment to be provided by general	- ()
	practitioner	5 (0.3%)
	Discharged – did not require any follow-up treatment	9 (0.5%)
	Referred to A&E clinic	13 (0.7%)
A&E attendance	Referred to fracture clinic	1 (0.1%)
disposal - A&E	Referred to other outpatient clinic	1 (0.1%)
only	Transferred to other healthcare provider	28 (1.5%)
	Referred to other healthcare professional	6 (0.3%)
	Left department before being treated	1 (0.1%)
	Left department having refused treatment	0 (0.0%)
	Other	5 (0.3%)
	Not known	2 (0.1%)
	Died in department	1296 (67.3
	Missing	7 (0.4%)
	Least deprived 10%	126 (6.5%)
IMD 2004 index	Less deprived 10-20%	95 (4.9%)
	Less deprived 20-30%	139 (7.2%)
	Loss doprived 20,40%	120 (6.2%)

	Less deprived 40-50%	133 (6.9%)
	More deprived 10-20%	257 (13.3%)
	More deprived 20-30%	213 (11.1%)
	More deprived 30-40%	173 (9.0%)
	More deprived 40-50%	205 (10.6%)
	Most deprived 10%	459 (23.8%)
	HES Critical care	All
Length of level 2 C	C days	0.9 (1.7)
Length of level 3 C	C days	4.4 (5.4)
Total length of CC	days	6.6 (15.4)
	ICNARC CMP	All
Length of level 0 I	ΓU days	0 (0.3)
Length of level 1 I	۲U days	0.1 (0.6)
Length of level 2 I	ΓU days	1.1 (4.0)
Length of level 3 I	rU days	5.2 (9.4)
Total length of ITU	I days	6.5 (12.9)
Total length of I	TU days in 30 days survived patients	10.5 (22.0)
Total length of I	TU days in 30 days deceased patients	4.8 (4.5)
Days of alive and f	ree of ITU stay in the first 28 days of cardiac arrest	6.9 (10.3)
	Both withheld then withdrawn	23 (5.7%)
Treatment	Withheld	4 (1.0%)
withheld/withdrav	wn Withdrawn	133 (32.7%)
	Neither	247 (60.7%)
	Heartbeating solid organ donor	13 (3.2%)
	No solid organs or tissues	
Organ donation	donated	199 (48.9%)
ergan denation	Non-heartbeating solid organ	1 5 (2 70/)
	donor Ticsue deper only	13 (5.7%)
		8 (2.0%)
	Definite museardial information	
A alumination		
Diagnosis	Acute coronary syndrome	30 (10.5%)
Diagnosis	Chest pain cause	4 (2.2%)
		22 (12.1%)
	Missing	1 (0.5%)
	Cardiac care unit	94 (51.6%)
	Acute admissions unit	6 (3.3%)
	General medical ward	1 (0.5%)
Admission Ward	Intensive therapy unit	69 (37.9%)
	Other	9 (4.9%)
	Cardiac ward (non CCU)	1 (0.5%)
	Stepdown ward	0 (0.0%)
	Unknown	0 (0.0%)
	Died in A&E	1 (0.5%)

	Missing	3 (2.2%)
Initial	None	18 (13.19
Reperfusion	Thrombolytic treatment	0 (0.0%)
Treatment	pPCI in house	116 (84.
	Referred for consideration for pPCI elsewhere	0 (0.0%)
	Unknown	0 (0.0%)
	Missing	30(21.9%
Drocoduro	No angiogram	2 (1.5%)
performed	Angiogram but no PCI	9 (6.6%)
performed	Angiogram and PCI	96 (70.19
	Unknown	0 (0.0%)
	Missing	1(2.9%)
	Protocol driven investigation performed in this hospital	12(35.3%
	Symptom driven investigation performed in this hospital	7 (20.6%
	Protocol driven investigation performed at another hospital	0 (0.0%)
Coronary	Symptom driven investigation performed at another hospital	0 (0.0%)
angiography	Planned after discharge	0 (0.0%)
	Not applicable	9 (6.6%)
	Patient refused	1 (2.9%)
	Not performed	5 (14.7%
	Unknown	0 (0.0%)
	Missing	6 (17.6%
	Percutaneous coronary intervention	9 (26.5%
	CABG	0 (0.0%)
_	PCI planned after discharge	0 (0.0%)
Coronary	CABG planned after discharge	1(2.9%)
intervention	Not applicable	5 (14.7%
	Patient refused	1 (2.9%)
	Not performed or arranged	11 (32.49
	Unknown	0 (0.0%)
	Missing	5 (2.7%)
	No contact with a non interventional hospital	126 (69.2
	Patient remains in ambulance	0 (0.0%)
Assessment at	A&E	30 (16.59
non-	Acute assessment unit	2 (1.1%)
interventional	CCU / cardiac facility	1 (0.5%)
centre	Self referral	0 (0.0%)
	Already in hospital	2 (1.1%)
	Other	0 (0.0%)
	Unknown	16 (8.8%
	Missing	59 (32.49
Assessment at	Assessed in A&E	68 (37.49
interventional	Acute assessment unit	1 (0.5%)
centre		= (0.070)

	Catheter laboratory	28 (15.4%)
	Already in hospital	0 (0.0%)
	Unknown	0 (0.0%)
	NICOR PCI	All
Cardiopulmonary	Missing	29 (28.7%)
resuscitation	No	72 (71.3%)
(CPR)	Yes	0 (0.0%)
Coronary artery	Missing	0 (0.0%)
bypass grafting	No	101 (100%)
(CABG)	Yes	0 (0.0%)
	Missing	101 (100%)*
Ventilation	No	0 (0.0%)
	Yes	0 (0.0%)
	Missing	101 (100%)*
Hypothermia	No	0 (0.0%)
	Yes	0 (0.0%)
	Missing	101 (100%)
Percutaneous	No	0 (0.0%)
coronary	Yes	0 (0.0%)
intervention (PCI)	No	0 (0.0%)
	Yes	0 (0.0%)

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Supplementary Table 2: Summary of demographic and cardiac arrest event characteristics in trial patients with and without matched HES inpatient, Critical care and A&E data

		HES matched	HES unmatched	n value	
		N=2079	N=319		
Age (year)	Γ	73.6 (21.9)	71.8 (24.4)	0.151	
Sex	Male	1315 (63.3%)	215 (67.4%)	0.151	
	Female	764 (36.8%)	104 (32.6%)	0.151	
	Presumed cardiac	1786 (85.9%)	272 (85.3%)		
	Respiratory	146 (7.0%)	27 (8.5%)		
Initial aetiology	Submersion	8 (0.4%)	1 (0.3%)	0.864	
	Other	74 (3.6%)	9 (2.8%)		
	Unknown	65 (3.1%)	10 (3.1%)		
	VF	624 (30.0%)	99 (31.0%)		
	VT	20 (1.0%)	1 (0.3%)		
Initial rhythm	PEA	613 (29.5%)	83 (26.0%)	0.468	
	Asystole	727 (35.0%)	118 (37.0%)		
	Unknown	95 (4.6%)	18 (5.6%)		
	Home	1610 (77.4%)	206 (64.6%)		
Location	Public place	333 (16.0%)	89 (27.9%)	<0.001	
	Other	136 (6.5%)	24 (7.5%)		
	Not witnessed	508 (24.5%)	60 (18.8%)	0.027	
	By bystander	961 (46.3%)	170 (53.3%)		
	By EMS	413 (19.9%)	60 (18.8%)		
witness	By Non-EMS		4 (4 20()		
	healthcare	64 (3.1%)	4 (1.3%)		
	Unknown	132 (6.4%)	25 (7.8%)		
Cardiopulmonary	No	1104 (53.1%)	156 (48.9%)		
resuscitation	Yes	862 (41.5%)	144 (45.1%)	0 376	
(CPR) by Bystander	Unknown	113 (5.4%)	19 (6.0%)	0.570	
Response time (mi	inute)†	6.1 (4.3)	7.2 (5.1)	<.0001	
Survival at	Alive	224 (10.8%)	38 (11.9%)		
30days	Deceased	1855 (89.2%)	281 (88.1%)	0.544	
,	ROSC	790 (38.0%)	125 (39.2%)		
ROSC at hospital	CPR in progress	1204 (57.9%)	135 (42.3%)	<0.001	
transfer	Unknown	85 (4.1%)	59 (18.5%)		
FO5d at 3 months	Children	70.0 (20.0)	75.0 (20.0)	0.970	
EQ5d at 12 months		80.0 (30.0)	72.5 (26.0)	0.368	
SE12 mental health at 3 months		50.4 (16.8)	45.4 (23.0)	0.690	
SE12 physical heal	th at 3 months	40.8 (14.2)	44.1 (15.0)	0.533	
SF12 mental healt	h at 12 months	51.0 (14.5)	44.1 (10.5)	0.118	
SE12 physical heal	SF12 nhysical health at 12 months		38.4 (13.9)	0.059	
HADS Anxiety at 1	HADS Anviety at 12 months		6 5 (5 0)	0 112	
HADS Anxiety at 12 months		5.0 (7.0)	0.5 (5.0)	0.112	

HADS depression at 12 months	4.0 (5.0)	6.0 (4.5)	0.163
MMSE at 12 months	29.0 (3.0)	29.0 (2.0)	0.648
PTSD at 12 months	27.0 (17.0)	33.0 (19.0)	0.280

Note: Continuous variables were shown as median (Interquartile range) and categorical variables were shown as n (percentage). †: response time was from 999 call to EMS arrival at scene.

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Supplementary Table 3: Summary of demographic and cardiac arrest event characteristics in patients with matched HES Critical care only, CMP only and both.

		HES Critical	ICNARC CMP	Critical care &	n valuo
		Care only	only	СМР	p value
Age (year)		68.3 (24.6)	64.8 (28.2)	65.5 (21.2)	0.684
Sov	Male	36 (70.6%)	66 (63.5%)	208 (68.7%)	0 556
JEX	Female	15 (29.4%)	38 (36.5%)	95 (31.4%)	0.550
	Presumed cardiac	45 (88.2%)	84 (80.8%)	247 (81.5%)	
	Respiratory	1 (2.0%)	12 (11.5%)	25 (8.3%)	0 4
Aetiology	Submersion	0 (0.0%)	1 (1.0%)	1 (0.3%)	0.554
	Other	3 (5.9%)	6 (5.8%)	20 (6.6%)	
	Unknown	2 (3.9%)	1 (1.0%)	10 (3.3%)	
	Home	37 (72.6%)	68 (65.4%)	209 (69.0%)	
Location	Public place	14 (27.5%)	30 (28.9%)	79 (26.1%)	0.516
	Other	0 (0.0%)	6 (5.8%)	15 (5.0%)	
	No	11 (21.6%)	26 (25%)	69 (22.8%)	
	By bystander	29 (56.9%)	59 (56.7%)	174 (57.4%)	
Witness	By EMS	7 (13.7%)	13 (12.5%)	32 (10.6%)	0.981
Withess	By Non-EMS healthcare	1 (2.0%)	2 (1.9%)	9 (3.0%)	
	Unknown	3 (5.9%)	4 (3.9%)	19 (6.3%)	
Cardianulmananu	No	24 (47.1%)	45 (43.3%)	136 (44.9%)	0.802
resuscitation	Yes	24 (47.1%)	52 (50.0%)	155 (51.2%)	
resuscitation	Unknown	3 (5.9%)	7 (6.7%)	12 (4.0%)	
	VF	26 (51%)	44 (42.3%)	153 (50.5%)	
	VT	2 (3.9%)	1 (1.0%)	4 (1.3%)	
Rhythm	PEA	10 (19.6%)	25 (24.0%)	55 (18.2%)	0.437
	Asystole	11 (21.6%)	26 (25.0%)	80 (26.4%)	
	Unknown	2 (3.9%)	8 (7.7%)	11 (3.6%)	
Response time (mi	nute)†	6.6 (4.4)	6.7 (4.7)	6.0 (3.9)	0.034
Survival at	Alive	19 (37.3%)	31 (29.8%)	93 (30.7%)	0.000
30days	Deceased	32 (62.8%)	73 (70.2%)	210 (69.3%)	0.000
DOCC at been ital	ROSC	42 (82.4%)	79 (76%)	241 (79.5%)	
ROSC at nospital	CPR in progress	7 (13.7%)	14 (13.5%)	47 (15.5%)	0.294
transier	Unknown	2 (3.9%)	11 (10.6%)	15 (5.0%)	1
EQ5d at 3 months		67.5 (24.0)	75.5 (16.0)	70.0 (25.0)	0.838
EQ5d at 12 months		80.0 (14.0)	74.0 (20.0)	80.0 (25.0)	0.298
SF12 mental health at 3 months		48.4 (11)	48.3 (19.3)	49.3 (16.5)	0.794
SF12 physical health at 3 months		38.9 (13.2)	39.2 (13)	41.1 (14.2)	0.836
SF12 mental health	SF12 mental health at 12 months		43 (14.3)	47.8 (15.2)	0.543
SF12 physical health at 12 months		42.9 (21)	38.8 (14.6)	46.7 (15.6)	0.235

HADS Anxiety at 12 months	5.0 (5.0)	9.5 (6.5)	6.0 (6.0)	0.078
HADS depression at 12 months	4.0 (3.0)	6.0 (5.5)	5.0 (8.0)	0.368
MMSE at 12 months	28.0 (3.0)	29.0 (3.0)	29.0 (3.0)	0.717
PTSD at 12 months	30.0 (8.5)	40.0 (23.0)	29.0 (15.0)	0.631

Note: Continuous variables were shown as median (Interquartile range) and categorical variables were shown as frequency (percentage). †: response time is from 999 call to EMS arrival at scene.

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Feasibility of data linkage in the PARAMEDIC Trial: a cluster randomised trial of mechanical chest compression in out of hospital cardiac arrest

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- 1 Word count
- 2 Abstract: 280
- 3 Main body: 3554 (excluding Tables/Figures/titles/notes/legends)

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1		
2	1	Abstract
4	-	
5	2	Objectives: There is considerable interest in reducing the cost of clinical trials. Linkage of trial data to
6	3	administrative datasets and disease-specific registries may improve trial efficiency, but has not been
7	۵ ۵	reported in resuscitation trials conducted in the LIK. To assess the feasibility of utilising national
8	5	administrative and clinical datasets to follow up natients transported to bosnital following
9	5	attempted resuscitation in a cluster randomised trial of a mechanical chest compression device in
10	7	out of hospital cardiac arrost (OHCA)
12	/	out of hospital caldiac affest (OFICA).
13	8	Methods: Hospital data on trial participants were requested from Hospital Episode Statistics (HES);
14	9	the Intensive Care National Audit and Research Centre (ICNARC): and Myocardial Ischaemia National
15	10	Audit Project (MINAP) and National Audit of Percutaneous Coronary Intervention (NAPCI) using
16	11	unique patient identifiers. Linked data were received between June 2014 and June 2015
/ 10	11	
10	12	Results: Of 4471 patients randomised in the PARAMEDIC trial, 2398 (53.6%) were not known to be
20	13	deceased at emergency department arrival and were eligible for linkage. We achieved an overall
21	14	match rate of 86.7% in the combined HES A&E, inpatient and Critical care dataset, with variable
22	15	match rates (4.2-80.4%) in individual datasets. Patient demographics, cardiac arrest related
23	16	characteristics and major outcomes were predominantly similar between HES matched and
24	17	unmatched groups, in the linkage apart from location, response time and ROSC at handover.
23 26		
27	18	Conclusions: This study shows that it is feasible to track patients from the pre-hospital setting
28	19	through to hospital admission using routinely available administrative datasets with a moderate to
29	20	high degree of success. This approach has the potential to complement the trial data with the
30	21	demographic and clinical management information about the studied cohort, as well as to improve
31	22	the efficiency and reduce the costs of follow-up in cardiac arrest trials.
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1 Strengths and limitations of this study

- First study evaluating the supplement of routinely collected administrative data in a cardiac arrest trial in the UK.
- Data linkage was made to different UK national registries.
- The matching reliability was suboptimal due to relaxed matching criteria, matching method and possible data quality issues.
- Routine data were not fully available for all trial patients transported to hospital.
- The findings of our study are not generalisable to facilitate trial recruitment since it was • considered unrealistic in the clinical context of cardiac arrest. to occurrence on the second

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1 Background

Well conducted and reported randomised controlled trials (RCTs) are considered the gold standard in evaluation of new or established clinical interventions. In cardiac arrest resuscitation science, only a small minority (1%) of contemporary international guideline recommendations are based on the highest level of evidence from more than one RCT, meta-analysis of high quality RCTs, or RCTs corroborated by high quality registry studies.¹ High quality trials to address outcomes of interest to patients following cardiac arrest (e.g. long term survival, neurocognitive status and disability)² are complex, labour intensive and expensive to perform. Many studies in cardiac arrest are therefore too small or inadequately conducted (with a predominance of observational studies which are prone to bias) to provide reliable estimates of treatment effect or harm to patients. Consequently, for the majority of resuscitation interventions, there is a paucity of high quality evidence. Funders (typically government agencies) have called for proposals for low-cost, more efficient trials.³

Traditional trial methods of patient tracking and data access in individual hospitals is challenging with limited resources. Cardiovascular medicine has attempted to improve the efficiency of the trial design by pioneering the concept of registry-based randomised trials, using clinical quality registries and administrative datasets. In the Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction (TASTE) trial, undertaken in Sweden, both patient enrolment and follow up were conducted using the Swedish Web System for Enhancement and Development of Evidence-based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry.⁴ On publication, this registry-based trial was hailed as the 'next disruptive technology' in clinical research, and as a new clinical trial paradigm.^{5 6} Subsequent registry-based trials have been reported in a comparison of radial versus femoral access in women undergoing percutaneous coronary intervention in the United States,⁷ and of supplemental oxygen versus ambient air in patients with suspected acute myocardial infarction in Sweden.⁸

To our knowledge, however, there are no reports of registry-based randomised trials in resuscitation science. However, should accessing registry data to ascertain outcomes in a prehospital cardiac arrest trial (e.g. length of stay/patient pathways/survival status) to be feasible, this could be one way of significantly improving efficiency and reducing costs of conducting high quality randomised trials in resuscitation.

30 In the PARAMEDIC trial, the in-hospital data collection process was complex, expensive and labour 31 intensive, with research paramedics visiting multiple hospitals across large geographical areas to 32 extract data from hospital records. Patients transported to hospital following resuscitation from 33 cardiac arrest follow multiple clinical pathways depending on their clinical status and treatments. As

hospital data are routinely collected and managed by national registries, utilising these registries
 could save resources and time in the in-hospital data collection and potentially reduce the burden
 on patients and relatives in the sensitive period following cardiac arrest.

4 This paper reports our assessment of the feasibility of linking data collected for the purposes of 5 patient follow up in a pragmatic, cluster randomised controlled trial of a mechanical chest 6 compression device undertaken in the United Kingdom (UK) prehospital setting, with large national 7 administrative and specialist registries.

8 Methods

The PARAMEDIC trial examined the effectiveness of LUCAS-2, a mechanical chest compression device, in 4471 patients with out of hospital cardiac arrest (OHCA). The study was a cluster randomised trial whereby emergency medical service (EMS) vehicles were randomised to carry the LUCAS-2 device (intervention) or not (control). Full details of the trial protocol have been published previously.⁹ In summary, adults with OHCA where resuscitation was attempted by EMS personnel and attended by a trial vehicle were included. Patients with traumatic cardiac arrest or suspected to be pregnant were excluded. Trial recruitment ran from April 15, 2010 to June 10, 2013. We have previously reported primary outcome (30-day survival),¹⁰ secondary outcomes,¹¹ an economic analysis¹² and characteristics of patients who were not resuscitated.¹³

18 Data sources

The PARAMEDIC trial utilised four sources of data that were linked to the trial dataset: UK National Health Service (NHS) Hospital Episodes Statistics (HES), Myocardial Ischaemia National Audit Project (MINAP),¹⁴ National Audit of Percutaneous Coronary Interventions (NAPCI),¹⁵ and Case Mix Programme (CMP)¹⁶ to obtain data on hospital stay and treatment or procedures that trial patients received in hospital.

We used the MINAP, NAPCI and CMP data for the health economic analysis¹² and long-term post admission outcomes¹¹ and to validate the hospital length of stay or stay in the intensive care (secondary outcomes for the efficacy part of the trial), and also to gain insight into the specifics of the treatment or procedures that trial patients received during their hospital stay. Characteristics of the registries are summarised in Table 1.

29 Table 1: Characteristics of registries, participation and case ascertainment.

Registry/Dataset Source Description case ascertainm during the trial	Registry/Dataset	Source	Description	Participation and case ascertainment during the trial per
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Paramedic trial	Warwick Clinical Trials Unit	Trial patient cohort that survived admission to a hospital	n/a
Hospital Episode Statistics (HES)	NHS Digital (NHSD)	Collection of information on all NHS hospital inpatients, Accident and Emergency (A&E), critical care and outpatients which enables health care providers to be paid according to their levels of activity.	All hospitals Case ascertainment 100%
Case Mix Programme (CMP)	Intensive Care National Audit and Research Centre (ICNARC)	Audit of patient outcomes from all adult, general critical care units in England, Wales and Northern Ireland. Other specialist units, including neurosciences, cardiac and high dependency units, also participate	Over 90% of critical care units Case ascertainment not reported
Myocardial Ischaemia National Audit Project (MINAP)	National Institute for Cardiovascular Outcomes Research (NICOR)	National audit of patients with acute coronary syndrome admitted to all hospitals in England, Wales and Northern Ireland. Data are collected prospectively at each hospital by secure electronic system, electronically encrypted and transferred online to a central database	All hospitals Case ascertainment not reported
NAPCI (National Audit of Percutaneous Coronary Interventions)	National Institute for Cardiovascular Outcomes Research (NICOR)	National audit of all PCI procedures from NHS and non-NHS hospitals in the United Kingdom.	All hospitals Case ascertainment 97%

1 Note: *: Case ascertainment – Rate (e.g. %) of eligible cases included in a registry/database.

2 Patient population

3 Patients (denominator) for this linkage study were patients from the PARAMEDIC trial who were

4 transported to hospital by EMS and not known to be deceased (i.e. documented as alive or unknown

5 status) on arrival at the emergency department (ED).

6 Since NHS Digital, responsible for HES, only provides annual data up to 1st April each year, no data on

7 trial patients recruited on or after 1st April 2013 had any HES data returned for this data request. We

8 therefore limited our analysis of the linked registry data to patients recruited to the PARAMEDIC trial
9 between April 2010 and March 2013.

Study approvals

The PARAMEDIC trial was approved by the Coventry Research Ethics Committee (reference 09/H1210/69) and sponsored by the University of Warwick, UK. The study was conducted in accordance with the principles of Good Clinical Practice and the Mental Capacity Act (2005). Specific approval for access to personal data without consent and the data linkage reported in this paper was obtained from the Confidentiality Advisory Group, part of the Health Research Authority (reference:

1 ECC 2-02 (c)/2011). At the time of the study this activity was undertaken by the National Information

2 Governance Board for Health and Social Care Ethics and Confidentiality Committee.

3 Patient and public involvement

Patient and public representatives (PPR) were invited to the Trial Steering Committee meetings during the development and conduct of the main trial. They agreed with the data collection via linkage to reduce the burden on patients and relatives. They were regularly informed of this study and other trial outputs. The results of this study will be disseminated in different ways, including presentation on the publicly accessible trial webpage.

9 Data linkage procedure

Data access applications were submitted to national administrative and disease registries between 2012-2014 to request patient case mix and clinical variables (Supplementary Table 1). The following patient identifiers were sent to the NHSD, ICNARC and NICOR to identify their clinical records: trial number, cardiac arrest date, ambulance service case number, 999 call time, hospital name, hospital arrival time, hospital handover time, patient name, NHS number, home address and postcode. The trial data were linked to the two NICOR datasets (MINAP and NAPCI) on two separate occasions by a different member of NICOR staff, which reassuringly generated the same results. Extracted anonymous data were encrypted and sent back to the trial team between June 2014 and June 2015.

Linked data may contain multiple, non-event related hospital records within the requested linkage period. We firstly used patient cardiac arrest (trial event) date to identify the records with exactly matched admission/visit date in the respective data sources. However, event and admission dates could be different due to potential data definition discrepancies. For instance, a trial event could occur before midnight and the patient was admitted to hospital after midnight. Therefore, we relaxed the date match criterion to a 5-day range (date of cardiac arrest with +/- 2 days). A matched record was redefined as if the admission/visit date falls in the range. We considered the range would be sufficiently large to mitigate against any date discrepancies in different sources and also be reasonably small to reduce the chance of mismatch in the case of early re-admission. Where multiple records could be matched to a single trial event in the same routine dataset, separate rules were used to extract the retrieved information: 1) where a patient had multiple episodes in HES, only the one with recorded death or discharge date was retained. If a patient had not been discharged from hospital, the episode with latest ward admission date was used. 2) Where multiple admissions to ICU were recorded in CMP, only the first ICU admission was linked to a trial event. 3) Since the MINAP dataset provided to us by NICOR only contained year and month of admission, only the earliest admission was used. 4) Only the first procedure was included for the linkage to the

2	1	NARCH assistent data, since watights are basic more than and intermediated and due (and thus
3 4	1	NAPCI registry data, since patients can have more than one interventional procedure (and thus
4 5	2	another record) during the index admission.
6		
7	3	Data linkage rate
8 9	4	For HES data, we developed the linkage and match rate for linked and matched (or correctly linked)
10	5	cases as follows:
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12	6	
13 14		
15	7	HES linkage rate = <u>N of patients with linked HES inpatient, Critical care or A&E data</u>
16	8	N of patients not known to be deceased at ED
17	9	
18	10	HES match rate = N of nations with matched (correctly linked) HES inpatient. Critical care or A&E data
19 20	11	N of patients not known to be deceased at ED
21	12	
22		
23	13	Similar equations were used to determine the rates for each of the datasets i.e. MINAP, NAPCI and
24	14	CMP. As we were not able to confirm which patient should actually be collected in these datasets.
25 26	4 5	
20	15	we employed same denominator used in the above equations.
28	16	Data linkaga guality
29	10	Natch rank is an indicator used in UEC to show the confidence of match, 1 suggests the best match
30	17	Match rank is an indicator used in HES to show the confidence of match. I suggests the best match
32	18	and 8 the worst. Level 1-3 appear to be of high quality as cases are matched based on a combination
33	19	of unique NHS number and data of date of birth, sex and home postcode. The quality of linkage in
34 35	20	matched HES was therefore summarised on the basis of percentage of level 1-3.
36		
37	21	Data representativeness
38	22	Data representativeness was assessed in two comparisons. The first comparison intended to assess
39 40	23	whether the patients with correctly linked (i.e. matched) HES data could be representative of the
41	24	trial population. It was carried out in patients with and without matched HES inpatient, Critical Care
42 43	25	or A&E data (comparison 1). The second comparison intended to assess the difference between two
44	26	critical care data sources. We were not able to compare data from these two sources directly as
45 46	27	some patient care data were collected in both databases. Hence, we split the patients by their linked
47	28	data sources and made the comparison between patients with HES Critical Care only, with CMP data
48 49	20	only and with both HES Critical Care and CMP data (comparison 2)
50	25	only and with both hes entited care and eivin data (comparison 2).
51	30	For both comparisons, we compared patient and event characteristics between the datasets.
52 53	31	Continuous variables were compared using Mann-Whitney test in comparison 1 and Kruskal-Wallis
54	32	test in comparison 2. Categorical variables were compared using Chi-square test. A two-sided p
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56 57		
58		0
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1 value <0.05 was considered statistically significant. All analyses were conducted in SAS v9.3 (Cary,

2 NC, USA).

3 Data security and destruction

4 We followed the Warwick Clinical Trials Unit Standard Operating Procedures (SOPs) for data storage,

- 5 transfer, and data sharing. The data were retained and destroyed in accordance with relevant
- 6 regulations and the University of Warwick's Data Sharing Agreements.

Results

- 8 In the PARAMEDIC trial, 2695 patients were transported to hospital and not known to be deceased
- 9 at ED. Of these 2398 (89.0%) were recruited between April 2010 and March 2013 and were
- 10 therefore included in this study (referred to as "linkage patients"). The data requests to NHSD,
- 11 ICNARC and NICOR retrieved different numbers of patient clinical records.

12 Summary of the linkage

- 13 The flow chart of the linkage to HES is shown in Figure 1. The linkage patients were grouped into ICU
- 14 admitted (patients with matched HES Critical care data) and not admitted (patients with other
- 15 matched HES data). Meanwhile, patients with matched CMP data were also summarised in the
- 16 flowchart. This presented a comparison between CMP and HES Critical Care. 303 patients were
- 17 matched in both CMP and HES Critical Care. Overall, the linkage to HES data achieved a match rate
- 18 of 86.7% (2079 of 2398) with allowed variation in dates (date of cardiac arrest with +/- 2 days),
 - 19 slightly improved from the use of exact date match approach (84.1%).
- 20 Linkage quality was high in matched cases: level 1-3 accounted for 97.9%. In unmatched cases,
- 21 91.5% (292 of 319) had no linked HES data and the rest, while linked with non-trial even related
- 22 data, had a good match rank (<=3).
 - The summary of linkage and match rate in each dataset are shown in Table 2. All datasets contained multiple linked records, indicating some patients had been linked to multiple admissions with possible multiple episodes. Among the 2398 linkage patients, individual match rate varied depending on the hospitalisation stage and received treatments. HES A&E had the highest individual match rate (80.4%). In the patients admitted to ICU, CMP provided 53 more matched patients with a lower
- 28 proportion of unmatched data in linked patients compared to HES Critical Care.

30 Figure 1: Linkage match rate and flowchart of patients retrieving HES or CMP data.

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3 Table 2: Summary of linked PARAMEDIC trial patients to the respective registry databases

Data source	Dataset	Number of linked records	Number of linked patients (linkage rate)*	Number of matched patients (match rate)*
NHSD	HES Inpatient	12875	1617 (67.4%)	771 (32.2%)
	HES Critical care	545	433 (18.1%)	354 (14.8%)
	HES A&E 📉	6434	2186 (91.2%)	1927 (80.4%)
	Overall	19854	2277 (95.0%)	2079 (86.7%)
ICNARC	СМР	435	410 (17.1%)	407 (17.0%)
NCAP	MINAP	244	218 (9.1%)	182 (7.6%)
	PCI	153	128 (5.3%)	101 (4.2%)

Note: *: Percentage is calculated using the number in the column divided by 2398 linkage patients.

A summary of retrieved information for each linked dataset as well as the degree of data missingness for each field is available in the online supplementary materials. In Supplementary Table 2, the trial patients that had not been matched to the HES records were similar to those that with matched records in age (mean age 71.8 and 73.6 respectively), male (67.4% and 63.3% respectively were male). They were also similar between groups in initial cardiac arrest aetiology where most were of cardiac origin (85.3% and 85.9% respectively) and in initial rhythm (shockable rhythm 31.0% and 31.3%). Patients with unmatched data were more likely to have had a cardiac arrest in a public place (27.9%) compared with of those with matched records (16%), witnessed by bystander (53.3% versus 46.3%) and had longer EMS response time (7.2 versus 6.1 minutes). Supplementary Table 3 illustrates the comparison of demographic and event characteristics of patients with matched HES Critical Care and CMP data. Characteristics were similar in all three groups, except for a significant difference in the EMS response time.

18 Discussion

This study aimed to demonstrate the feasibility of collecting trial outcome data during patient follow up in a prehospital cardiac arrest trial via linkage to national registries. We achieved an overall match rate of 86.7% in 2398 patients using HES data. The data linkage provided important administrative and additional clinical data that allowed extended analyses of the intervention effect and provided more details of patient journey in the trial. We also evaluated the representativeness of retrieved HES and CMP data by comparing patient and trial event characteristics. No substantial difference

was found in patients with and without matched HES inpatient, Critical Care or A&E data, as well as in patients with matched HES Critical Care only, CMP only and both datasets.

This was the first study evaluating the supplement of routinely collected administrative data in a cardiac arrest trial in the UK. Our match rate was in line with observational studies linking EMS data to hospital records,¹⁷⁻²⁰ and data validation studies.²¹ Our experience suggests it is feasible to obtain relevant data from administrative databases in a cardiac arrest trial. In addition to the high match rate reported in this paper, the matched data are deemed to be sufficiently representative of the trial population. The comparison between patients with and without matched HES showed low level of imbalance of event characteristics. We have found similar results in the matched ICU data.

The unmatched cases were likely to be associated with missing or inaccurate data. Data quality could be at increased risk due to the challenging circumstances of cardiac arrest and complexity of patient handling following hospital arrival. In addition, routine data in the chosen registries are not systematically adjudicated. Lack of clinical engagement may compromise the case ascertainment and data quality,²² leading to suboptimal linkage. NHS Digital employs deterministic and probabilistic methods in the data linkage. The latter calculates probability weight based on combinations of linkage variables and determines linkage based on a cut-off threshold. Although this method largely improves the linkage, it could incorrectly link record pairs and miss valid ones, undermining the reliability of linkage.

Linkage to individual routine datasets resulted in variable match rates. HES A&E generated the highest rate of 80.4% as most patients were taken by EMS to ED for assessment before being admitted to specialist hospital units. Other rates reflected the proportion of specific groups of patients in the linkage. The CMP, MINAP and NAPCI registries are focused on selected patients with a specific diagnosis and/or requiring specialist care, reflected in strict inclusion and exclusion criteria; for example MINAP comprises data on patients with suspected and/or confirmed acute coronary syndrome, NAPCI on interventional cardiology whilst CMP registry collects data on patients admitted to critical care/intensive care units within any given hospital. In this study, MINAP and NAPCI generated 9.1% and 5.3% respectively. Patients who die in the ED are less likely to be recorded on MINAP, and only those patients receiving interventional cardiology are recorded in NAPCI.

Use of routine data has the potential to reduce the costs of conducting trials. The cost of the TASTE trial was reported as US\$300,000, or approximately \$50 per patient,⁴ 2 per cent of the cost of a traditional randomised trial, but differs from the PARAMEDIC trial in that we did not use registry data to identify and recruit patients in the challenging and time-pressured setting of our-of-hospital cardiac arrest. In the West of Scotland Coronary Prevention (WOSCOPS) trial, data linkage reduced

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costs of long term follow up to less than one per cent of trial budget.²³ However, the time cost of
linkage could be unrealistic for some trials. Linkage for the PARAMEDIC trial took up to three years
from application to the trial team obtaining the data. It has been suggested that NHS Digital, who
performed the linkage to HES for our study was overwhelmed with data linkage applications.²⁴ This
may limit the usefulness of administrative data in trials with funder-imposed deadlines for
completion.

7 Limitations:

8 Our study had several limitations. The matching reliability was suboptimal due to relaxed matching 9 criteria (using range of event date), matching methods and potential issues of data quality and completeness, common to administrative data. Bohensky et al.²⁵ conducted an evidence synthesis of 10 data linkage studies and identified factors such as sub-optimal or incomplete linkage leading to 11 12 systematic bias. They considered the participant or population characteristics that can influence the 13 validity and completeness of data linkage and may in turn lead to systematic bias in reporting. They 14 reported variation in quality of data linkage across geographical/hospital sites, which could be due to 15 high staff turnover or not sufficient resources allocated to the data collection and/or coding. We 16 have not considered such variations in this study, but overall match quality was high in the matched 17 cases.

18 Secondly, routine data were not fully available for all patients transported to hospital. Some patients 19 were not included in the linkage as their data were not available in HES at the time of our data 20 application. Although no substantial bias was shown, the generalisability of results could be limited. 21 Several data fields were incomplete, for example, MINAP captures most ST elevation myocardial 22 infarction (STEMI) cases but data for non-STEMI are less complete. We also cannot confirm how 23 many patients required specialist care and should be included in non-HES datasets. Therefore, we 24 were unable to assess and report the impact of unmatched cases in in the linkage to these registries. 25 Thirdly, we used the first matched admission without considering repeated or later admissions. We 26 were therefore unlikely to fully describe patients' hospital pathway based on matched information. 27 Fourthly, our focus for the present study was on assessing the feasibility of using administrative data 28 for purposes of follow-up. We did not assess the utility of administrative data to facilitate 29 recruitment of trial patients since this was considered unrealistic in the clinical context of cardiac 30 arrest.

Fifthly, we did not assess the financial cost of manual data collection at hospitals to compare with
the cost of the use of registries in the trial linkage.

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1 Recommendations

Based on our experience, we made the following recommendations to improve the use of datalinkage in trials:

4	1.	When planning a trial using linkage to administrative registries, careful planning is required
5		to assess availability of the required data. Linkage to routine data in different jurisdictions or
6		multiple registries requires separate applications for data release and may be subject to data
7		availability.
8	2.	Trialists need to be mindful of prolonged processes for regulatory approvals, data release
9		and validation. These processes may extend beyond trial funding.
10	3.	Data linkage is a lengthy often unpredictable process in the application stage, possibly due
11		to the restricted capacity of registries funded primarily to assess quality of care. Most
12		registries in the NHS are funded as national audits and do not have sufficient resources for
13		the timely processing of data sharing requests.
14	4.	The quality of routinely collected data in the national registries may be inferior to that
15		collected using traditional trial processes. Registry data are collected in high volume with
16		limited resources and the validation process is unlikely to be as robust as in trials that are
17		better resourced. Moreover, collected variables in registries are reviewed periodically and
18		may change to reflect advances in clinical practice, which can impact on data completeness.
19		Therefore, we suggest that trialists use registry data as the main source of all in-hospital
20		data points and active data collection by a study team as an auxiliary approach to collect
21		data for the unmatched patients.
22	5.	It is common for registries to charge a fee for data release, which should be costed in to trial
23		budgets.

Conclusions

This study shows that it is feasible to track patients from the pre-hospital setting through to hospital admission using routinely available administrative datasets with a moderate to high degree of success. This may improve the efficiency and reduce the costs for longer-term follow-up in cardiac arrest trials.

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1 Declaration of interests

2 GDP, RL, TQ, CDD and SG report grants from NIHR HTA Programme during the conduct of the study.

3 The other authors declare no competing interests.

4 Author's contributions

CS, JH, SG and GDP led on the data linkage. CJ analysed data. CJ, TQ and LG drafted the manuscript
with input from the co-authors; RL, CS, JH, CDD, HP, MAS, NR, SJM, SG and GDP reviewed the
manuscript. All authors approved the final version.

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- 20 Data sharing statement

21 No additional data sharing available.

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Supplementary materials:

	HES Inpatient	All
CSK operation	No	606 (79.6%)
CSK Operation	Yes	155 (20.4%)
	The usual place of residence, including no fixed abode	192 (24.9%)
	Temporary place of residence when usually resident elsewhere	4 (0.5%)
	Repatriation from high security psychiatric hospital (from 1999-2000)	0 (0.0%)
	Repatriation from high security psychiatric hospital (from 1999-2000)	0 (0.0%)
	Penal establishment - court (from 1999-2000)	0 (0.0%)
	Penal establishment - police station (from 1999-2000)	0 (0.0%)
	Penal establishment - court and police station excluded (from 1999-2000 to 2006-07)	0 (0.0%)
	High security psychiatric hospital, Scotland (from 1999-2000)	0 (0.0%)
	NHS other hospital provider - high security psychiatric accommodation	0 (0.0%)
	NHS other hospital provider - medium secure unit (from 1999- 2000)	32 (4.2%)
	NHS other hospital provider - ward for maternity patients or neonates	0 (0.0%)
Destination of	NHS other hospital provider - ward for patients who are mentally	0 (0 0%)
discharge		0 (0.0%)
	NHS run nursing nome, residential care nome or group nome	3 (0.4%)
	provided (from 1996-97)	0 (0.0%)
	Local authority foster care, but not in Part 3 residential accommodation - where care is provided (from 1996-97)	0 (0.0%)
	LA home or care (1989-90 to 1995-96)	0 (0.0%)
	Non-NHS run hospital - medium secure unit (from 2003-04)	1 (0.1%)
	Non-NHS (other than local authority) run residential care home (from 1996-97 to 2003-04) and care home (from 2003-04)	3 (0.4%)
	Non-NHS (other than local authority) run nursing home (from 1996-97 to 2003-04)	0 (0.0%)
	Non-NHS run hospital	0 (0.0%)
	Non-NHS (other than local authority) run hospice	2 (0.3%)
	Non-NHS institution (1989-90 to 1995-96)	0 (0.0%)
	Not applicable	7 (0.9%)
	Not known	1 (0.1%)
	Died	522 (67.7%)
Method of	Discharged on clinical advice or with clinical consent	234 (30.4%)
discharge	Self discharged, or discharged by a relative or advocate	5 (0.6%)

Supplementary Table 1: Summary of retrieved information in each linked dataset.

	Secretary or a court	0 (0.0%)
	Baby was still born	0 (0.0%)
	Not applicable: patient still in hospital	10 (1.3%)
	Not known: a validation error	0 (0 0%)
	Died	522 (67 79
	Missing	94 (10 Q%
	Logst deprived 10%	64 (10.3%)
	Least deprived 10.20%	04 (0.570)
	Less deprived 10-20%	45 (5.0%)
	Less deprived 20-50%	47 (0.1%)
IND 2004 index	Less deprived 40 50%	35 (4.5%)
IND 2004 Index	Less deprived 40-50%	50 (6.5%)
	More deprived 10-20%	80 (10.4%
	More deprived 20-30%	84 (10.9%
	More deprived 30-40%	58 (7.5%)
	More deprived 40-50%	61 (7.9%)
	Most deprived 10%	165 (21.4%
Hospital length of	stay*	7.7 (20.3)
	HES A&E	All
	Emergency departments	1865 (96.8
N&E denartment	Consultant-led mono specialty accident and emergency service'	0 (0.0%)
type - A&F only	Other type of A&E. Excludes NHS walk-in centres	4 (0.2%)
type nationly	NHS walk-in centres	1 (0.1%)
	Not known	57 (3.0%)
	Admitted to hospital bed / became a lodged patient of the same	
	health care provider	560 (29.1%
	Discharged – follow-up treatment to be provided by general	
	practitioner	5 (0.3%)
	Discharged – did not require any follow-up treatment	9 (0.5%)
	Referred to A&E clinic	13 (0.7%)
A&E attendance	Referred to fracture clinic	1 (0.1%)
disposal - A&E	Referred to other outpatient clinic	1 (0.1%)
only	Transferred to other healthcare provider	28 (1.5%)
	Referred to other healthcare professional	6 (0.3%)
	Left department before being treated	1 (0.1%)
	Left department having refused treatment	0 (0.0%)
	Other	5 (0.3%)
	Not known	2 (0.1%)
	Died in department	1296 (67.3
	Missing	7 (0.4%)
	Least deprived 10%	126 (6.5%
IMD 2004 index	Less deprived 10-20%	95 (4.9%)
	Less deprived 20-30%	139 (7.2%

	Less deprived 40-50%	133 (6.9%)
	More deprived 10-20%	257 (13.3%)
	More deprived 20-30%	213 (11.1%)
	More deprived 30-40%	173 (9.0%)
	More deprived 40-50%	205 (10.6%)
	Most deprived 10%	459 (23.8%)
	HES Critical care	All
Length of level 2 C	C days	0.9 (1.7)
Length of level 3 C	C days	4.4 (5.4)
Total length of CC	days	6.6 (15.4)
	ICNARC CMP	All
Length of level 0 IT	TU days	0 (0.3)
Length of level 1 IT	TU days	0.1 (0.6)
Length of level 2 IT	TU days	1.1 (4.0)
Length of level 3 IT	TU days 🔪 📃	5.2 (9.4)
Total length of ITU	days	6.5 (12.9)
Total length of I	TU days in 30 days survived patients	10.5 (22.0)
Total length of I	TU days in 30 days deceased patients	4.8 (4.5)
Days of alive and f	ree of ITU stay in the first 28 days of cardiac arrest	6.9 (10.3)
	Both withheld then withdrawn	23 (5.7%)
Treatment	Withheld	4 (1.0%)
withheld/withdraw	vn Withdrawn	133 (32.7%)
	247 (60.7%)	
	Heartbeating solid organ donor	13 (3.2%)
	No solid organs or tissues	
Organ donation	donated	199 (48.9%)
0	Non-heartbeating solid organ	15 (3.7%)
		8 (2 0%)
		8 (2.078)
	Definite myocardial infarction	126 (69 2%)
Admission		30 (16 5%)
Diagnosis	Chest pain cause	4 (2.2%)
Diagnosis	Other initial diagnosis	22 (12 1%)
	Missing	1 (0 5%)
	Cardiac care unit	94 (51.6%)
		6 (3 3%)
	General medical ward	1 (0 5%)
	Intensive therapy unit	69 (37 9%)
Admission Ward	Other	9 (1 9%)
	Cardiac ward (non CCII)	1 (0 5%)
	Stendown ward	
		1 (U.3%)

None	18 (13.1%)
Thrombolytic treatment	0 (0.0%)
pPCI in house	116 (84.7%
Referred for consideration for pPCI elsewhere	0 (0.0%)*
Unknown	0 (0.0%)
Missing	30(21.9%)
No angiogram	2 (1.5%)
Angiogram but no PCI	9 (6.6%)
Angiogram and PCI	96 (70.1%)
Unknown	0 (0.0%)
Missing	1(2.9%)
Protocol driven investigation performed in this hospital	12(35.3%)
Symptom driven investigation performed in this hospital	7 (20.6%)
Protocol driven investigation performed at another hospital	0 (0.0%)
Symptom driven investigation performed at another hospital	0 (0.0%)
Planned after discharge	0 (0.0%)
Not applicable	9 (6.6%)
Patient refused	1 (2.9%)
Not performed	5 (14.7%)
Unknown	0 (0.0%)
Missing	6 (17.6%)
Percutaneous coronary intervention	9 (26.5%)
CABG	0 (0.0%)
PCI planned after discharge	0 (0.0%)
CABG planned after discharge	1(2.9%)
Not applicable	5 (14 7%)
Patient refused	1 (2.9%)
Not performed or arranged	11 (32,4%)
	0 (0 0%)
Missing	5 (2,7%)
No contact with a non interventional hospital	126 (69 2%
Patient remains in ambulance	0 (0 0%)
A&F	30 (16 5%)
Acute assessment unit	2 (1.1%)
CCU / cardiac facility	1 (0 5%)
Self referral	0 (0 0%)
Already in hospital	2 (1 1%)
Other	
	16 (8 8%)
Micsing	50 (22 /0/)
	68 (27 10/)
Asita assassment unit	
	1 1 1 1 0 . 5 701
-	None Thrombolytic treatment pPCI in house Referred for consideration for pPCI elsewhere Unknown Missing No angiogram Angiogram but no PCI Angiogram and PCI Unknown Missing Protocol driven investigation performed in this hospital Symptom driven investigation performed at another hospital Protocol driven investigation performed at another hospital Symptom driven investigation performed at another hospital Planned after discharge Not applicable Patient refused Not performed Unknown Missing Percutaneous coronary intervention CABG PCI planned after discharge CABG planned after discharge Not performed or arranged Unknown Missing No contact with a non interventional hospital Patient refused Not contact with a non interventional hospital Patient remains in ambulance A&E Acute assessment unit CCU / cardiac facility Self re

	Catheter laboratory	28 (15.4%)
	Already in hospital	0 (0.0%)
	Unknown	0 (0.0%)
	NICOR PCI	All
Cardiopulmonary	Missing	29 (28.7%)
resuscitation	No	72 (71.3%)
(CPR)	Yes	0 (0.0%)
Coronary artery	Missing	0 (0.0%)
bypass grafting	No	101 (100%)
(CABG)	Yes	0 (0.0%)
	Missing	101 (100%)*
Ventilation	No	0 (0.0%)
	Yes	0 (0.0%)
	Missing	101 (100%)*
Hypothermia	No	0 (0.0%)
	Yes	0 (0.0%)
	Missing	101 (100%)
Percutaneous	No	0 (0.0%)
coronary	Yes	0 (0.0%)
intervention (PCI)	No	0 (0.0%)
	Yes	0 (0.0%)
	ere added to the dataset after the linkage was performed.	

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Supplementary Table 2: Summary of demographic and cardiac arrest event characteristics in trial patients with and without matched HES inpatient, Critical care and A&E data

		HES matched	HES unmatched	n value	
		N=2079	N=319	p value	
Age (year)	1	73.6 (21.9)	71.8 (24.4)	0.151	
Sov	Male	1315 (63.3%)	215 (67.4%)	0 151	
JEX	Female	764 (36.8%)	104 (32.6%)	0.151	
	Presumed cardiac	1786 (85.9%)	272 (85.3%)		
	Respiratory	146 (7.0%)	27 (8.5%)		
Initial aetiology	Submersion	8 (0.4%)	1 (0.3%)	0.864	
	Other	74 (3.6%)	9 (2.8%)		
	Unknown	65 (3.1%)	10 (3.1%)		
	VF	624 (30.0%)	99 (31.0%)		
	VT	20 (1.0%)	1 (0.3%)		
Initial rhythm	PEA	613 (29.5%)	83 (26.0%)	0.468	
	Asystole	727 (35.0%)	118 (37.0%)		
	Unknown	95 (4.6%)	18 (5.6%)		
	Home	1610 (77.4%)	206 (64.6%)		
Location	Public place	333 (16.0%)	89 (27.9%)	<0.001	
	Other	136 (6.5%)	24 (7.5%)		
	Not witnessed	508 (24.5%)	60 (18.8%)	0.027	
	By bystander	961 (46.3%)	170 (53.3%)		
Witness	By EMS	413 (19.9%)	60 (18.8%)		
Withess	By Non-EMS	64 (3.1%)	A (1.3%)		
	healthcare	04 (3.176)	4 (1.376)		
	Unknown	132 (6.4%)	25 (7.8%)		
Cardiopulmonary	No	1104 (53.1%)	156 (48.9%)		
resuscitation	Yes	862 (41.5%)	144 (45.1%)	0.376	
(CPR) by Bystander	Unknown	113 (5.4%)	19 (6.0%)		
Response time (m	inute)†	6.1 (4.3)	7.2 (5.1)	<.0001	
Survival at	Alive	224 (10.8%)	38 (11.9%)	0 5 4 4	
30days	Deceased	1855 (89.2%)	281 (88.1%)	0.544	
	ROSC	790 (38.0%)	125 (39.2%)		
ROSC at nospital	CPR in progress	1204 (57.9%)	135 (42.3%)	<0.001	
transier	Unknown	85 (4.1%)	59 (18.5%)	1	
EQ5d at 3 months		70.0 (20.0)	75.0 (20.0)	0.970	
EQ5d at 12 month	S	80.0 (30.0)	72.5 (26.0)	0.368	
SF12 mental health at 3 months		50.4 (16.8)	45.4 (23.0)	0.690	
SF12 physical heal	th at 3 months	40.8 (14.2)	44.1 (15.0)	0.533	
SF12 mental healt	h at 12 months	51.0 (14.5)	44.1 (10.5)	0.118	
SF12 physical heal	th at 12 months	45.2 (17.4)	38.4 (13.9)	0.059	
HADS Anxiety at 1	2 months	5.0 (7.0)	6.5 (5.0)	0.112	

HADS depression at 12 months	4.0 (5.0)	6.0 (4.5)	0.163
MMSE at 12 months	29.0 (3.0)	29.0 (2.0)	0.648
PTSD at 12 months	27.0 (17.0)	33.0 (19.0)	0.280

Note: Continuous variables were shown as median (Interquartile range) and categorical variables were shown as n (percentage). +: response time was from 999 call to EMS arrival at scene.

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Supplementary Table 3: Summary of demographic and cardiac arrest event characteristics in patients with matched HES Critical care only, CMP only and both.

		HES Critical	ICNARC CMP	Critical care &	n valuo
		Care only	only	СМР	p value
Age (year)		68.3 (24.6)	64.8 (28.2)	65.5 (21.2)	0.684
Sov	Male	36 (70.6%)	66 (63.5%)	208 (68.7%)	0 556
Sex	Female	15 (29.4%)	38 (36.5%)	95 (31.4%)	0.550
	Presumed cardiac	45 (88.2%)	84 (80.8%)	247 (81.5%)	
A - 1 ¹ - 1	Respiratory	1 (2.0%)	12 (11.5%)	25 (8.3%)	0.554
Aetiology	Submersion	0 (0.0%)	1 (1.0%)	1 (0.3%)	0.554
	Other	3 (5.9%)	6 (5.8%)	20 (6.6%)	
	Unknown	2 (3.9%)	1 (1.0%)	10 (3.3%)	
	Home	37 (72.6%)	68 (65.4%)	209 (69.0%)	
Location	Public place	14 (27.5%)	30 (28.9%)	79 (26.1%)	0.516
	Other	0 (0.0%)	6 (5.8%)	15 (5.0%)	
	No	11 (21.6%)	26 (25%)	69 (22.8%)	
	By bystander	29 (56.9%)	59 (56.7%)	174 (57.4%)	
Witness	By EMS	7 (13.7%)	13 (12.5%)	32 (10.6%)	0.981
Withess	By Non-EMS healthcare	1 (2.0%)	2 (1.9%)	9 (3.0%)	
	Unknown	3 (5.9%)	4 (3.9%)	19 (6.3%)	
Candianulmannanu	No	24 (47.1%)	45 (43.3%)	136 (44.9%)	0.802
resuscitation	Yes	24 (47.1%)	52 (50.0%)	155 (51.2%)	
resuscitation	Unknown	3 (5.9%)	7 (6.7%)	12 (4.0%)	
	VF	26 (51%)	44 (42.3%)	153 (50.5%)	
	VT	2 (3.9%)	1 (1.0%)	4 (1.3%)	
Rhythm	PEA	10 (19.6%)	25 (24.0%)	55 (18.2%)	0.437
	Asystole	11 (21.6%)	26 (25.0%)	80 (26.4%)	
	Unknown	2 (3.9%)	8 (7.7%)	11 (3.6%)	
Response time (mi	nute)†	6.6 (4.4)	6.7 (4.7)	6.0 (3.9)	0.034
Survival at	Alive	19 (37.3%)	31 (29.8%)	93 (30.7%)	0 606
30days	Deceased	32 (62.8%)	73 (70.2%)	210 (69.3%)	0.000
	ROSC	42 (82.4%)	79 (76%)	241 (79.5%)	0.294
ROSC at nospital	CPR in progress	7 (13.7%)	14 (13.5%)	47 (15.5%)	
transier	Unknown	2 (3.9%)	11 (10.6%)	15 (5.0%)	
EQ5d at 3 months		67.5 (24.0)	75.5 (16.0)	70.0 (25.0)	0.838
EQ5d at 12 months		80.0 (14.0)	74.0 (20.0)	80.0 (25.0)	0.298
SF12 mental health at 3 months		48.4 (11)	48.3 (19.3)	49.3 (16.5)	0.794
SF12 physical health at 3 months		38.9 (13.2)	39.2 (13)	41.1 (14.2)	0.836
SF12 mental health at 12 months		51.6 (8)	43 (14.3)	47.8 (15.2)	0.543
SF12 physical health at 12 months		42.9 (21)	38.8 (14.6)	46.7 (15.6)	0.235

HADS Anxiety at 12 months	5.0 (5.0)	9.5 (6.5)	6.0 (6.0)	0.078
HADS depression at 12 months	4.0 (3.0)	6.0 (5.5)	5.0 (8.0)	0.368
MMSE at 12 months	28.0 (3.0)	29.0 (3.0)	29.0 (3.0)	0.717
PTSD at 12 months	30.0 (8.5)	40.0 (23.0)	29.0 (15.0)	0.631

Note: Continuous variables were shown as median (Interquartile range) and categorical variables were shown as frequency (percentage). †: response time is from 999 call to EMS arrival at scene.

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STROBE Statement—checklist of items that should be included in reports of observational studies

 a) Indicate the study's design with a commonly used term in the title or the abstract b) Provide in the abstract an informative and balanced summary of what was done and what was found Explain the scientific background and rationale for the investigation being reported Explain the scientific background and rationale for the investigation being reported Explain the scientific background and rationale for the investigation being reported Explain the scientific background and rationale for the investigation being reported Explain the scientific background and rationale for the paper Present key elements of study design early in the paper Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls 	1 3 5-6 6 6 6-7 7	
 b) Provide in the abstract an informative and balanced summary of what was done and what was found Explain the scientific background and rationale for the investigation being reported Explain the scientific objectives, including any prespecified hypotheses Present key elements of study design early in the paper Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case inscertainment and control selection. Give the rationale for the choice of cases and controls 	3 5-6 6 6-7 7	
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participants		
b) Cohort study—For matched studies, give matching criteria and number of exposed and	Not applicable	
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Case-control study—For matched studies, give matching criteria and the number of controls per		
case		
Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers.	9	
Give diagnostic criteria, if applicable		
For each variable of interest, give sources of data and details of methods of assessment	6-7	
measurement). Describe comparability of assessment methods if there is more than one group		
Describe any efforts to address potential sources of bias	8	
Explain how the study size was arrived at	6, 10 (figure 1)	
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Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	9
variables		groupings were chosen and why	
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	9
methods		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Not applicable
		(d) Cohort study-If applicable, explain how loss to follow-up was addressed	Not applicable
		Case-control study—If applicable, explain how matching of cases and controls was addressed	
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling	
		strategy	
		(<u>e</u>) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible,	6-7
		examined for eligibility, confirmed eligible, included in the study, completing follow-up, and	
		analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	10 (figure 1)
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on	Supplementary
data		exposures and potential confounders	table 2
		(b) Indicate number of participants with missing data for each variable of interest	Supplementary
			table 1&2
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study-Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	10-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	10-11,
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	Supplementary
		included	table 1-3
		(b) Report category boundaries when continuous variables were categorized	Not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	Not applicable
		period	

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Prevention 11-12 initiations 10 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss 11-12 interpretation 20 Ore acautious overall interpretation of results considering objectives, limitations, multiplicity of 11-14 interpretation 20 Discuss the generalisability (external validity) of the study results 31-14 Definition 10 Discuss the generalisability (external validity) of the study results 11-14 inding 20 Ore the source of funding and the ore of the funders for the present study and, if applicable, for the 15 original study on which the present article is based 0 Ore acationability of the save control studies and, if applicable, for the present studies. 0 Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies. 0 Give information 0 Discussion 0 0 Give information 0 Discussion Discussion 0 Give information 0 Discussion Discussion Discussion Give information 0 Discussion Discussion Discussion D	Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable		
Key results 18 Summarise key results with reference to study objectives 11-12 initiations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss 4, 13 interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 11-14 interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 11-14 interpretation 20 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based 13 Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies. Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.	Discussion					
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