Leeds Institute of Health Sciences
FACULTY OF MEDICINE AND HEALTH

UNIVERSITY OF LEEDS

WORKING PAPER NUMBER: WP18_4

Risk predictors of out of hospital cardiac arrest. Evidence from linked trial and national administrative data

Authors: Robert Willans (1), Silviya Nikolova (2), Claire Hulme (2), Ranjit Lall (3), Tom Quinn (4), Gavin Perkins (3,5)

(1) Bradford Teaching Hospitals NHS Foundation Trust
(2) Academic Unit of Health Economics, Leeds
(3) Warwick Clinical Trials Unit, University of Warwick
(4) Faculty of Health, Social Care and Education, Kingston University London and St.George's University of London
(5) Heart of England, NHS Foundation Trust

Corresponding author Silviya Nikolova, Academic Unit of Health Economics, Leeds, s.k.nikolova@leeds.ac.uk

This working paper should cited as: Willans et al.. Risk predictors of out of hospital cardiac arrest. Evidence from linked trial and national administrative data, AUHE WP18_04. University of Leeds, Leeds, 2018, Last modified 21/02/2018. Available from: URL

Worsley Building
University of Leeds
Leeds, United Kingdom
LS2 9JT

http://medhealth.leeds.ac.uk/lihs

Additional information

Funding This research was funded by the National Institute for Health Research Health Technology Assessment Programme (Award Number 07/37/69). The PARAMEDIC trial is registered on the International Standard Randomised Controlled Trial Number Register, ISRCTN08233942.

Conflict of interest The authors have no conflict of interest to declare

Acknowledgements The views and opinions expressed therein are those of the authors and do not reflect those of the NHS or the Department of Health.

Abstract

Objective To understand the demographic, health and healthcare (HC) use profile of patients who experience an out-of-hospital cardiac arrest (OHCA) in England and Wales between April 2010 and June 2013. The association with 24-hour survival was studied as a secondary objective.

Methods The Paramedic study is a trial which collected information on 4471 patients with out-of-hospital cardiac arrest (OHCA). Trial data was linked to Hospital Episode Statistics (HES), administrative data covering the trial period. Multivariate survival analysis was used to quantify the impact of identified risk predictors.

Results Healthcare use increases in the years leading up to a cardiac arrest with the profile of this increase differing depending on age and overall healthcare resource utilisation of the patient. Patients who are older than 60 were found to have 2.35 fold increase in the probability of not surviving OHCA. However, older patients with medium and high healthcare resource use have higher chances of surviving OHCA event (decrease in mortality risk of 67% and 70% respectively). A diagnosis of dementia carries a 3.1 fold increase in mortality risk.

Conclusions Routinely collected administrative hospital data may be used to identify patients at risk of OHCA and thus may help decrease cardiovascular mortality

Key words: OHCA, survival, predictors, healthcare use, health

JEL classification: I1

Introduction

Cardiac arrests are commonly the result of a myocardial infarction (MI) that then gives rise to a heart arrhythmia and the cessation of blood circulation. Though cardiac arrests and myocardial infarctions are different medical events, the risk factors and prodromal symptoms for cardiac arrest are related to those for MI. Many risk factors have been identified for cardiac arrest and myocardial infarction. Aside from the well-known factors elevating risk such as high blood pressure, smoking either personally or passively(1), and a sedentary lifestyle, other factors have been noted in the literature including kidney disease (2, 3) and anxiety (4). More immediate prodromal symptoms for cardiac arrest and MI include chest pain, gastrointestinal symptoms, fatigue, nausea and shortness of breath (5, 6). Difficulties for recognition arise as these symptoms are also often present in patients who do not go on to have an MI or arrest. There is also evidence that symptoms can present differently for women suffering an MI who are less likely to experience intense chest pain (7).

Previous research has described and analysed patterns of healthcare consumption or treatment prior to a cardiac event, noting an increase in healthcare contacts prior to the cardiac event (5, 8, 9). Forsling et al (10) found that healthcare contacts were higher in the week prior to MI event, though most patients did not have any health contacts. Weeke et al (9) found that younger patients were more likely to seek healthcare services than those in middle age or older.

Survival analysis of out of hospital cardiac arrest examining immediate emergency care variables has shown improved outcomes for cases where emergency medical staff were present prior to the event, and where CPR was administered promptly either by a bystander or emergency medical technician(11) and where the patient has a shockable heart rhythm(12).

The existing evidence focuses on prodromal factors and healthcare consumption patterns in the period immediately prior to OHCA (<30 days) using data with a small look-back window. Our study contributes to the body of knowledge by identifying risk factors and describing patterns of consumption in Admitted Patient Care (APC), Outpatient (OP) and Accident & Emergency) (AE) services over a three-year period prior to OHCA by using routinely collected hospital administrative data. It also studies separately survivors and non-survivors.

Methods

Data sets

The PARAMEDIC study collated a dataset of 4471 participants who suffered a cardiac arrest event between April 2010 and June 2013, outside of a hospital setting across sites in England and Wales (13, 15). The objective of the PARAMEDIC trial was to evaluate whether the introduction of LUCAS-2 (mechanical chest decompression device) into frontline emergency response vehicles would improve survival from OHCA. The study team also conducted a health economic evaluation of the intervention. The results of the trial and economic evaluation are reported in the PARAMEDIC report and paper (15, 16). As part of the trial, mortality information was recorded for each participant.

For the purposes of health economics evaluation trial data was linked to hospital administrative data (HES). HES contains details of all admissions, outpatient appointments and AE attendances at NHS hospitals in England. These data include attendance details, clinical details, and a rich set of individual characteristics. Importantly, different years of HES data can be linked allowing for healthcare use over time to be studied. This creates up to 3-years' worth of healthcare use data prior to OHCA.

Data preparation and analysis

HES records for the PARAMEDIC participants were obtained for the period between 01/04/10 and 31/3/13, covering NHS financial years 2010/11, 2011/12, and 2012/13. After merging trial data set with HES, data on 487 PARAMEDIC participants whose arrest took place between 01/04/13 and 10/06/13 was omitted from analysis, due to them occurring after the HES cut-off point of 31/3/13. The HES data for the remaining 3984 patients was then analysed to evaluate healthcare contacts and consumption in the period prior to the arrest.

Our main outcome measure is survival at 24 hours following cardiac arrest. Although one day survival rates are higher than survival at 30 days used in the trial analysis, they were preferred here as they isolate the effects of post-arrest healthcare consumption.

To understand healthcare use prior to OHCA we construct sample means, test their equivalence and plot utilisation through time. We enquire whether intensity of healthcare use changes prior to OHCA and what impact it has on survival. We look separately at APC, OP and AE healthcare use. We also explore the impact of age on survival and how patterns of healthcare consumption change for different age deciles.

A Cox proportional hazard model was used to analyse patterns of healthcare usage prior to arrest. This approach allows us to determine which predictors significantly increase the risk of death having suffered an arrest. The variables were predominantly drawn from International Classification of Diseases (ICD) diagnosis codes and Operating Procedure Codes (OPCS) generated on admissions to hospital. Variables were selected which represented comorbidities that may be present, variables that were associated with emergency cardiac treatment, and demographic factors such as age and social deprivation which may have an effect on survival. Each of the comorbidity/treatment variables were dummy variables constructed from the presence of that characteristic in an admitted care spell prior to the cardiac arrest event.

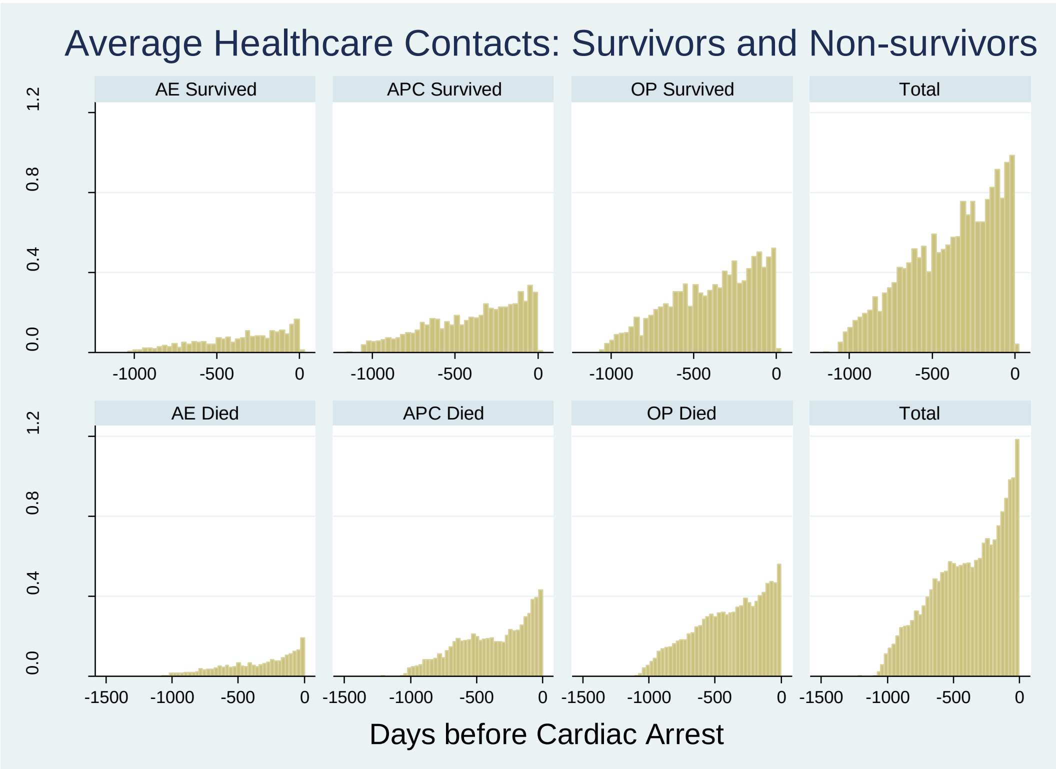
To determine variables for analysis, univariate Cox models are initially estimated. We then take the variables which come out as significant at the 20% confidence level and use them in multivariate regression.

Results

810 trial participants or approximately 20 % of the sample survived for at least 24 hours following the cardiac event. There are 3174 who died within this time period. Descriptive analysis of healthcare use prior to the arrest shows that those who survived had higher numbers of healthcare contacts prior to the arrest (73% increased number of Accident & Emergency (AE) attendances, 380% increased spells of admitted patient care (APC), and 68% increase in the mean number of outpatient appointments (OP).

We plot healthcare utilisation through time to explore change in healthcare consumption prior to the cardiac event. To account for different number of trial participants at each time point the usage is normalised by the number of participants at that time period. This is plotted against time to MI event which is denoted as 0 on the x-axis.

Graph 1: Average Healthcare Contacts: Survivors and Non-survivors



Graph 1 shows change over time in normalised AE, APC, OP and overall healthcare use for survivors and those who did not survive the cardiac event. The distribution of healthcare resource usage for both, survivors and non-survivors, is skewed right with a long tail of participants with large numbers of health contacts.

We also investigate whether intensity of healthcare use has predictive power of surviving a MI event. To this end the sample is divided into those without any healthcare usage prior to the arrest, and for those with recorded healthcare usage, subdivided into tertiles of “low”, “medium”, and “high” usage. The criterion for the split was the number of healthcare contacts weighted by the average NHS Reference Cost in 2014-15 for that mode of presentation (APC, OP, AE).

Table 1 shows cohort averages for survivors and non-survivors. We first note that the percentage of survivors grows with increase in number of pre-OHCA visits from 7.6% (143/1872) for participants with no healthcare usage, to 22.9 (162/706) for low use and to 34.4% (241/700) and 37.4% (264/706) for high use and medium use cohorts respectively. Second, within a cohort, higher OP and AE numbers are associated with lower probability of survival, although the difference in usage is statistically significant at the 5% level only for the medium HC use category. With regards to APC stays, higher numbers are associated with somewhat higher probability of survival, but the difference in means is statistically significant only for the low use category.

.

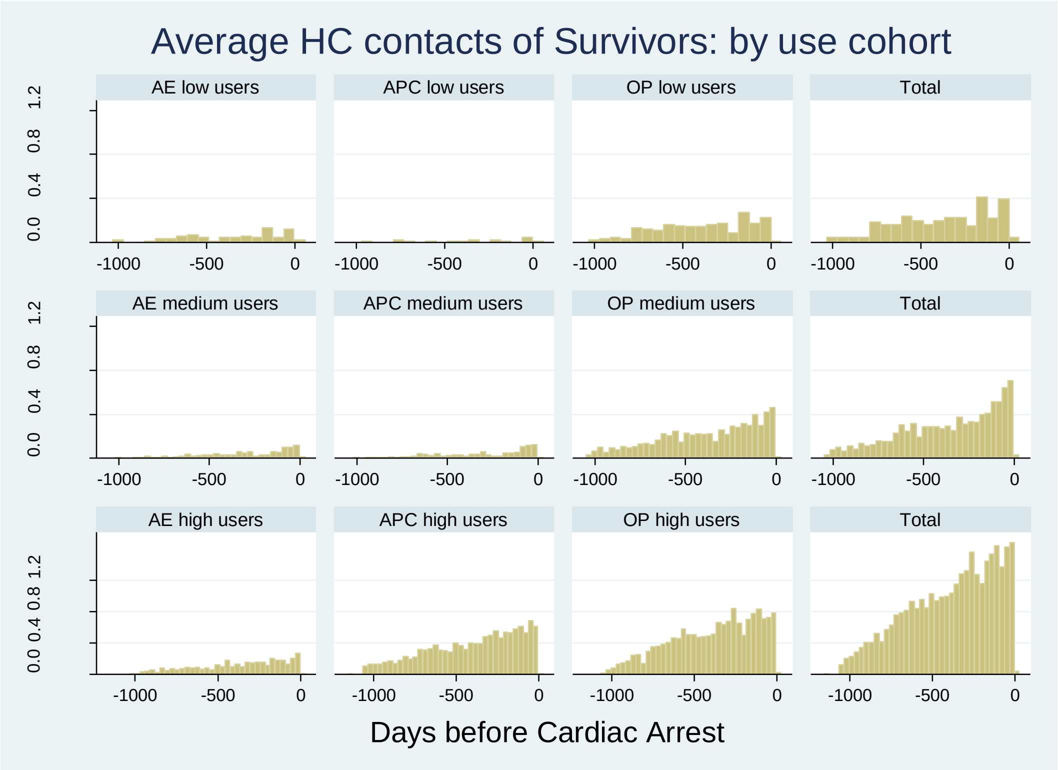
Table 1: Average healthcare use for Survivors and Non-Survivors by use cohort.

Healthcare Resource Use	None (n=1872)		Low (n=706)		Medium (n=706)		High (700)	
	Survived (n=143)	Did not Survive(n=1729)	Survived (n=162)	Did not Survive (n=544)	Survived (n=)264	Did not Survive (n=442)	Survived (n=241)	Did not Survive (n=459)
Admitted Patient Care	0	0	**0.76**	**0.55**	**2.23**	**1.88**	13.69	15.95
Outpatient	0	0	1.25	1.70	**5.81**	**8.67**	15.59	16.87
A&E	0	0	1.3	1.26	**1.8**	**2.19**	4.42	5.00

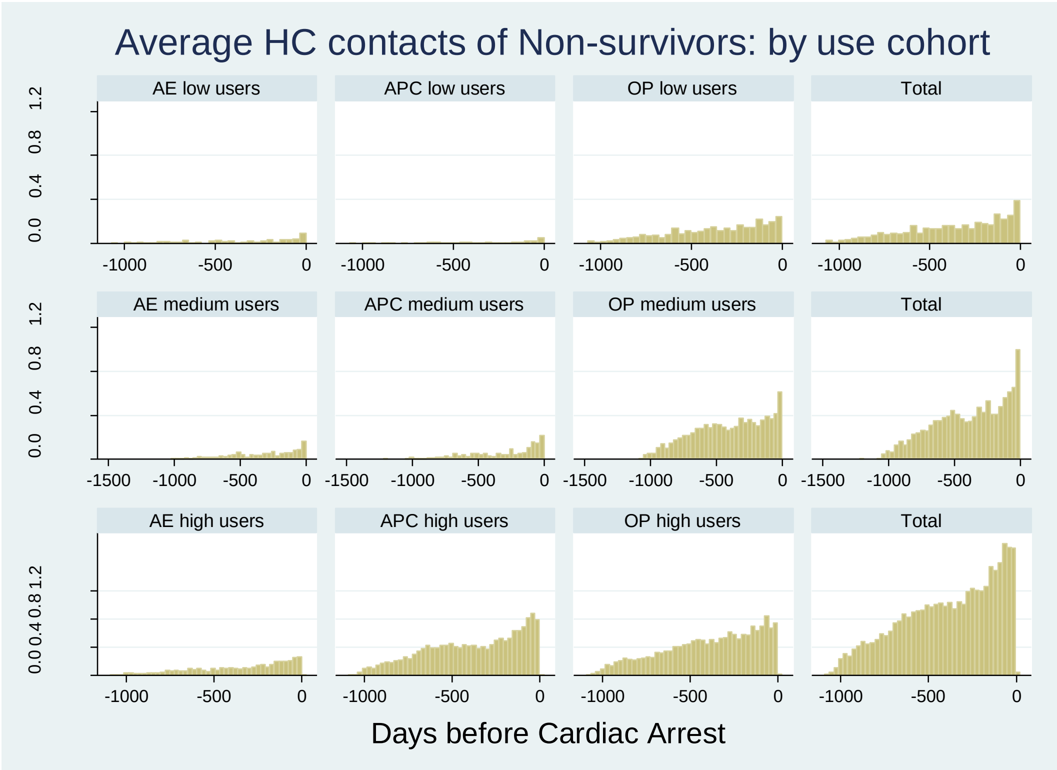
*number pairs in bold indicate statistical significance at the 5% CL.

We next plot average number of contacts for low, medium and high use cohort over time. Graphs 2 and 3 show that individuals in the low usage cohort, survivors and non-survivors, typically experience increase in the outpatient visits. Plots of healthcare use for those in the medium category show increases for all categories of healthcare prior to the event, though numbers for AE and APC use are small. The cohort of high healthcare use patients appear to make up the vast majority of healthcare contacts over the study period with a marked spike prior to the cardiac arrest event.

Graph 2: Average HC contacts of survivors: by use cohort



Graph 3: Average HC contacts of non-survivors: by use cohort



Previous research has identified age as one of the predictors of survival following a MI event (14). To explore its impact we split the sample into those with and without health resource use prior to MI. In Table 2 we present results for six age bands: <50, 50-59, 60-69, 70-79, 80-89 and 90+. It shows that, for participants with no healthcare usage, the probability of survival decreases with age from 11.2% (21/187)) for those who are less than 50 year old to 4.7% (14/298) for those above 90. For participants with healthcare contacts prior to MI Table 2 presents averages for APC, OP and AE visits. Test for mean equivalence shows that only OP visit means for survivors and non-survivors in the 50-59 age group are statistically different with higher number of OP visits associated with lower probability of survival. Also, for participants older than 60 most resource means are close in value. Similarly to the no healthcare use category, probability of survival decreases with age from 40% (107/267) for those who are less than 50 years old to 23% (42/181) for those above 90. The latter three observations suggest that, within age category, probability of survival is not associated with different healthcare resource use except for the 50-59 year olds where higher OP use correlates with not surviving a MI event.

Table 2 also suggests that spikes in healthcare consumption prior to the MI event (Graph 3) cannot be driven by age solely. Because differences in utilisation are statistically important only for the 50-59 age category age effect on utilisation is likely to be nonlinear.

Table 2: Average healthcare use for Survivors and Non-Survivors by age band and health resource use

Healthcare Resource Use		<50 (n=454)		50-59 (n=367)		60-69 (n=666)		70-79 (n=961)		80-89 (n=1055)		90+ (n=479)	
No HC resources used		Survived (n=21)	Did not survive (n=166)	Survived (n=17)	Did not survive (n=131)	Survived (n=28)	Did not survive (n=256)	Survived (n=33)	Did not survive (n=409)	Survived (n=30)	Did not survive (n=483)	Survived (n=14)	Did not survive (n=284)
HC resources used		Survived (n=107)	Did not survive (n=160)	Survived (n=80)	Did not survive (n=139)	Survived (n=127)	Did not survive (n=255)	Survived (n=157)	Did not survive (n=362)	Survived (n=154)	Did not survive (n=388)	Survived (n=42)	Did not survive (n=139)
	Admitted Patient Care	11.97	6.28	5.83	10.06	4.14	6.52	6.12	6.01	4.09	4.44	3.45	3.58
	Outpatient	6.27	7.36	**3.58**	**7.08**	9.31	8.67	10.93	11.33	8.44	8.27	8.02	5.72
	A&E	3.66	3.69	2.2	2.88	2.19	2.53	2.47	2.56	2.58	2.57	2.83	2.77

*number pairs in bold indicate statistical significance at the 5% CL

Additional exploratory analysis on the impact of age considers plots of healthcare use by age group[1]. The age plots reveal different patterns depending on age. Throughout the period leading up to the cardiac arrest event healthcare contacts for individuals below the age of 60 are dominated by APC visits. The pattern is different for individuals above the age of 60 with OP appointments dominating utilisation.

Univariate Cox results

Table 3 presents the statistical results from the univariate and multivariate Cox analysis. Within the univariate analyses, many of the coefficients for diagnosis related variables are negative. This may reflect that diagnosis would imply treatment for this and other conditions noted on admission. Dementia diagnosis is found to be statistically significant at the 5% level and increases the hazard ratio by 197%. An additional year of age led to an increase in the hazard ratio of 1%. The small magnitude of this increase is likely the reason why the effect of age was not detected in the exploratory analysis with six dummies. A decile increase in deprivation as measured by IMD increased the hazard ratio by 4%. An increase in the level of admitted care usage (as split out in table 2), was associated with an increase in the hazard ratio of 23%. Each additional procedure (defined as a simple count of OPCS codes per prior admitted care spell) carried out in a prior admitted healthcare visit reduced the hazard ratio by 17%.

Multivariate Cox results

Taking those variables which were found to be significant at the 20% level, a multivariate model was fitted with these variables. Because deprivation data is available for 43.9% of the sample and only 28 observations fall into the first healthcare use category, analysis is restricted to individuals with any healthcare utilisation to avoid small sample size problem.

We introduce a dummy for those above the age of 60 to account for the nonlinearities in the age effect suggested by the descriptive analysis. Interaction variables were used to isolate the effects of age on levels of healthcare usage. Healthcare use dummies are not included as separate explanatory variable as F-test showed these dummies to be jointly statistically insignificant. Local area deprivation is controlled by a set of decile dummies. Results for the final regression specification are presented in Table 5 below.

There is a 3.1 fold increase in the risk of death following cardiac arrest where a diagnosis of dementia was present and the effect is statistically significant. Deprivation has non-linear impact on survival with participants living in moderately deprived and very deprived neighbourhoods (decile 4, 6, 7 and 10) having better chances of survival than those in the least deprived areas. Individuals who are older than 60 experience 2.35 fold increase in the hazard of dying following OHCA and the effect is statistically significant. In our regression specification the baseline category is individuals who are

[1] For conciseness, these plots are not presented here and are available upon request.

older than 60 and have low healthcare use. We find that individuals who are older than 60 and have medium healthcare use have higher probability of survival compared to the baseline group. The coefficient estimate points to 67% statistically significant decrease in the hazard. For individuals who are older than 60 and have high healthcare use we find a statistically significant decrease in the hazard of 70% compared to the reference group. This finding indicates that, within a healthcare use category, age is predictive of survival with older people more likely to survive. The separate effect of healthcare use for medium and high healthcare use patients is found, respectively, to be a decrease of 22% and 21% (product of age and interaction coefficients).

Table 3: Statistical analysis

Variable	Hazard Ratio	Coefficient	P Value
Univariate analysis			
Diagnosed with Acute Myocardial Infarction	0.89	-0.12	0.71
Diagnosed with Congestive Heart Failure	0.79	-0.23	0.42
Diagnosed with Peripheral Vascular Disease	0.37	-0.99	0.09
Diagnosed with Cerebrovascular Disease	0.79	-0.23	0.59
Diagnosed with Dementia	2.97	1.09	0.00*
Diagnosed with COPD	0.72	-0.33	0.25
Diagnosed with Rheumatoid disease	0.95	-0.05	0.95
Diagnosed with Mild Liver Disease	0.78	-0.25	0.73
Diagnosed with Diabetes	0.77	-0.26	0.37
Diagnosed with Diabetes plus complications	0.49	-0.71	0.23
Diagnosed with Hemiplegia/Paraplegia	0.64	-0.44	0.66
Diagnosed with Renal Disease	0.78	-0.24	0.42
Diagnosed with Cancer	0.87	-0.14	0.70
Diagnosed with Severe Liver Disease	1.67	0.51	0.48
Diagnosed with Metastatic Cancer	1.57	0.45	0.39
Age (additional year)	1.01	0.13	0.00*
Level of deprivation in patient postcode (additional 10%)	1.04	0.04	0.00*

Additional level of admitted care usage (see table 2)	1.23	0.21	0.00*
Multivariate analysis			
Diagnosed with Peripheral Vascular Disease	0.47	-0.76	0.221
Diagnosed with Dementia	3.10	1.13	0.005*
Deprivation decile			
2	0.54	-0.62	0.313
3	0.77	-0.26	0.591
4	0.33	-1.10	0.098***
5	0.45	-0.81	0.218
6	0.20	-1.62	0.008*
7	0.33	-1.12	0.020**
8	0.43	-0.85	0.193
9	0.77	-0.27	0.587
10	0.30	-1.22	0.008*
Older than 60 dummy	2.35	0.85	0.06***
Interaction b/n age dummy and HC use category			
Older than 60 and medium HC use	0.33	-1.10	0.022**
Older than 60 and high HC use	0.30	-1.21	0.005*

Discussion

Healthcare usage increases prior to a cardiac arrest event, though the predictive power of monitoring health contacts is unclear. A prior diagnosis of dementia was associated with a significant increase in the risk of death following a cardiac arrest (Hazard Ratio 3.1). Age being greater than 60 at the time of the cardiac arrest was also associated with a significant increase in the risk of death. Where prior healthcare usage was at a medium or high level the risk was reduced.

Patients' higher contacts might be explained by the presence of other diseases rather than prodromal symptoms. However, frequent contact with healthcare services seemed to have protective effect with respect to OHCA.

We chose to analyse healthcare contacts in the 3-year period prior to OHCA because previous studies based on recall have found symptoms were experienced long before the cardiac arrest event.

Our results based on hospital administrative records are likely to be more precise as they do not carry the risk of recall bias.

A limitation of our analysis is that we do not have information on deprivation for all observations in the sample. As a result our deprivation results may be unreliable. We also have data only for individuals with OHCA. As a result, the patterns we observe in the data could not be unequivocally attributed to cardiac arrest event. However, our results regarding age and healthcare contacts concur with the findings from previous analysis (14, 10).

Conflicts of Interest

The authors have no conflict of interest to declare.

Acknowledgements

This research was funded by the National Institute for Health Research Health Technology Assessment Programme (Award Number 07/37/69). The PARAMEDIC trial is registered on the International Standard Randomised Controlled Trial Number Register, ISRCTN08233942.

References

1. Sargent, R.P., Shepard, R.M. and Glantz, S.A. Reduced incidence of admissions for myocardial infarction associated with public smoking ban: before and after study. *BMJ.* 2004, **328**(7446), pp.977-980.
2. Sarnak, M.J., Levey, A.S., Schoolwerth, A.C., Coresh, J., Culleton, B., Hamm, L.L., McCullough, P.A., Kasiske, B.L., Kelepouris, E., Klag, M.J., Parfrey, P., Pfeffer, M., Raij, L., Spinosa, D.J. and Wilson, P.W. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation.* 2003, **108**(17), pp.2154-2169.
3. Shamseddin, M.K. and Parfrey, P.S. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. *Nat Rev Nephrol.* 2011, **7**(3), pp.145-154.
4. Strik, J.J., Denollet, J., Lousberg, R. and Honig, A. Comparing symptoms of depression and anxiety as predictors of cardiac events and increased health care consumption after myocardial infarction. *J Am Coll Cardiol.* 2003, **42**(10), pp.1801-1807.
5. Hoglund, H., Jansson, J.H., Forslund, A.S. and Lundblad, D. Prodromal symptoms and health care consumption prior to out-of-hospital cardiac arrest in patients without previously known ischaemic heart disease. *Resuscitation.* 2014, **85**(7), pp.864-868.
6. Nishiyama, C., Iwami, T., Kawamura, T., Kitamura, T., Tanigawa, K., Sakai, T., Hayashida, S., Nishiuchi, T., Hayashi, Y. and Hiraide, A. Prodromal symptoms of out-of-hospital cardiac arrests: a report from a large-scale population-based cohort study. *Resuscitation.* 2013, **84**(5), pp.558-563.
7. McSweeney, J.C. and Crane, P.B. Challenging the rules: women's prodromal and acute symptoms of myocardial infarction. *Research in Nursing & Health.* 2000, **23**(2), pp.135-146.
8. Weeke, P., Folke, F., Gislason, G.H., Lippert, F.K., Olesen, J.B., Andersson, C., Fosbol, E.L., Charlot, M.G., Kanters, J.K., Poulsen, H.E., Nielsen, S.L., Kober, L. and Torp-Pedersen, C. Pharmacotherapy and hospital admissions before out-of-hospital cardiac arrest: a nationwide study. *Resuscitation.* 2010, **81**(12), pp.1657-1663.

9. Weeke, P., Folke, F., Gislason, G.H., Lippert, F.K., Olesen, J.B., Andersson, C., Wissenberg, M., Poulsen, H.E., Nielsen, S.L., Kober, L. and Torp-Pedersen, C. Hospital admissions and pharmacotherapy before out-of-hospital cardiac arrest according to age. *Resuscitation.* 2012, **83**(5), pp.584-590.
10. Forsling, E., Lundqvist, R., Eliasson, M. and Isaksson, R.M. Health care contact is higher in the week preceding a first myocardial infarction: A review of medical records in Northern Sweden in 2007. *European Journal of Cardiovascular Nursing.* 2015, **14**(5), pp.450-456.
11. Weston, C.F., Wilson, R.J. and Jones, S.D. Predicting survival from out-of-hospital cardiac arrest: a multivariate analysis. *Resuscitation.* 1997, **34**(1), pp.27-34.
12. Abrams, H.C., Moyer, P.H. and Dyer, K.S. A model of survival from out-of-hospital cardiac arrest using the Boston EMS arrest registry. *Resuscitation.* 2011, **82**(8), pp.999-1003.
13. Perkins, G.D., Lall, R., Quinn, T., Deakin, C.D., Cooke, M.W., Horton, J., Lamb, S.E., Slowther, A.-M., Woollard, M. and Carson, A. Mechanical versus manual chest compression for out-of-hospital cardiac arrest (PARAMEDIC): a pragmatic, cluster randomised controlled trial. *The Lancet.* 2015, **385**(9972), pp.947-955.
14. Herlitz J, Bång A, Gunnarsson J, et al. Factors associated with survival to hospital discharge among patients hospitalised alive after out of hospital cardiac arrest: change in outcome over 20 years in the community of Göteborg, *Sweden Heart.* 2003; **89**, pp25-30.

15 Gates S, Lall R, Quinn T, Deakin DC, Cooke MW, Horton J, et al, 2017. Prehospital randomised assessment of a mechanical compression device in out-of-hospital cardiac arrest (PARAMEDIC): a pramatic, cluster randomised trial and economic evaluation. Health Technology Assessment, **21**(11)

16 Marti J, Hulme C, Ferreira Z, Nikolova S, Lall R, Kaye C, Smyth M, Kelly C, Quinn T, Gates S, Deakin CD, Perkins GD. The cost-effectiveness of a mechanical compression devide in out-of-hospital cardiac arrest. Resuscitation, 2017; **117** (): 1-7