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Important factors in predicting mortality outcome from stroke: findings from the Anglia Stroke Clinical Network Evaluation Study

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Abstract

Background: although variation in stroke service provision and outcomes have been previously investigated, it is less well known what service characteristics are associated with reduced short- and medium-term mortality.
Methods: data from a prospective multicentre study (2009–12) in eight acute regional NHS trusts with a catchment population of about 2.6 million were used to examine the prognostic value of patient-related factors and service characteristics on stroke mortality outcome at 7, 30 and 365 days post stroke, and time to death within 1 year.
Results: a total of 2,388 acute stroke patients (mean (standard deviation) 76.9 (12.7) years; 47.3% men, 87% ischaemic stroke) were included in the study. Among patients characteristics examined increasing age, haemorrhagic stroke, total anterior circulation stroke type, higher prestroke frailty, history of hypertension and ischaemic heart disease and admission hyperglycaemia predicted 1-year mortality. Additional inclusion of stroke service characteristics controlling for patient and service level characteristics showed varying prognostic impact of service characteristics on stroke mortality over the disease course during first year after stroke at different time points. The most consistent finding was the benefit of higher nursing levels; an increase in one trained nurses per 10 beds was associated with reductions in 30-day mortality of 11–28% ($P < 0.0001$) and in 1-year mortality of 8–12% ($P < 0.001$).
Conclusions: there appears to be consistent and robust evidence of direct clinical benefit on mortality up to 1 year after acute stroke of higher numbers of trained nursing staff over and above that of other recognised mortality risk factors.

Keywords: *older people, stroke, services, staffing, outcome, mortality*

Introduction

Stroke is the one of the leading causes of death and the leading cause of long-term disability worldwide [1]. Langhorne *et al.* [2] demonstrated the clear clinical benefits of organised stroke unit care in their landmark systematic review, although the exact mechanisms for this effect were unclear. It appears that clinical benefits associated with stroke units are being observed up to 10 years post discharge [3]. Further work identified processes of care (e.g. therapy assessments) and management strategies (e.g. early mobilisation), and having access to facility (e.g. MRI) as characteristics of a stroke unit associated with a good outcome [4, 5].

Stroke care in United Kingdom is still far from ideal, patients having a worse outcome in terms of death and dependency than many other European countries [6–8], at least in part probably due to differences in care provided [9]. There is also variation in outcomes between different localities within the United Kingdom; results from a series of national stroke audits in the United Kingdom have repeatedly highlighted the differences in stroke services and care between hospitals and mortality outcome [10–12]. Examples of such differences include staffing levels, presence of early supported discharge, stroke specialist on call rota for thrombolysis and access to neurovascular/neurosurgical service [13].

Examination of the variation in stroke services and outcome in the UK setting could provide a valuable insight into which stroke service characteristics are associated with the best outcomes. This can only be achieved by assessment of the relationship between robustly collected detailed service level characteristics and relevant outcomes using representative observational sample taken into account of case-mix and access to care (e.g. urban vs rural setting). The study aimed to describe the regional variation in stroke mortality and to identify the characteristics of the services that were associated with better outcomes after accounting for case-mix differences and individual prognostic factors in a mostly rural population in East of England.

Methods

We conducted a cohort study in the East of England through the Anglia Stroke & Heart Clinical Network (ASHCN), with 1 year of follow-up after admission for stroke, or stroke while in hospital. The detailed description of the study has been previously reported [13]. Ethical approval was obtained from the NRES Committee East of England—Norfolk (REC Reference number 10/H0310/44). A consecutive sample of these patients was systematically selected in all eight acute NHS trusts in Norfolk, Suffolk and Cambridgeshire, with total catchment population of 2.6 million, between October 2009 and September 2011 [14].

Anonymised individual patient data on patients' prognostic factors on admission, health care received and mortality outcomes, as well as relevant characteristics of each provider organisation were collected prospectively. Baseline data on patients' prognostic characteristics on admission were prospectively recorded as a part of routine clinical data collection by ASHCN. Dates of death from any cause until 13 March 2013 were obtained by linkage with the NHS Central Register.

Data on the service capabilities and population and patient load of the eight units were also collected by research staff at each site. Information on the population served, staffing numbers and training at all levels and availability of essential clinical services was recorded at each site for each of four 6-month blocks spanning the 2 years in which stroke patient admissions were included in the study. For each field analysed, if a service characteristic at a site varied over the 2 years, then the mean of the values was used in the analysis.

Statistical analysis

Mortality outcome was examined at four time points: death within 7 (acute), 30 (sub-acute) or 365 days after admission (binary variables) (longer term) and time to death (with follow-up censored 365 days after admission). Analysis was conducted at individual patient level, with each patient also ascribed the characteristics of the stroke unit and hospital to which they were admitted. Intra-unit correlation of outcomes was accounted for using Huber-White robust adjustment [15].

First, we identified patient characteristics independently associated with above mortality outcome, using logistic regression or Cox-proportional hazards models as appropriate. The variables were selected based on well validated off the shelf stroke mortality predictors [16]. For Cox models, the proportionality of hazards during follow-up was assessed for each prognostic variable using complementary log–log plots. Second, we examined each characteristic of the stroke units separately, estimating its association with each outcome after adjustment for all of the prognostic variables selected in the first step. Staff to bed ratios were used in these analyses, because they are better indicators of the adequacy of staffing in each unit than are crude staff numbers. These ratios were expressed as whole time equivalent staff per 10 beds, which is a more realistic reflection of staffing levels in NHS stroke units than staff per single bed. Third, we modelled combinations of stroke unit characteristics, together with the same prognostic characteristics used in steps one and two. Stroke unit characteristics that were independently associated with each outcome were selected in the same way as prognostic characteristics selected in step one.

We excluded 4.3% of patients who were transferred between the sites because transferred patients tend to have more severe disease, so bias would be introduced depending on whether they were assigned to initial site or recipient site. We imputed missing prognostic data using multiple imputation with chained equations [17]. Ten data sets were created for each outcome, and regression results from each were combined using Rubin's rules [18]. Complete case sensitivity analyses were done, repeating all analyses but excluding anyone with any missing prognostic data. We estimated the proportion of outcome variance explained by each model, using pseudo R^2 for logistic regression models and Royston's R^2 for Cox models [19]. Analyses were performed using Stata SE 12.0 statistical software [20].

Results

Of 2,656 consecutive admissions during the study periods, after exclusion of 157 admissions with other diagnoses (see Supplementary data, available at *Age and Ageing* online), transfers (n = 108, 4.3%) and those with missing data for admission dates (n = 3, 0.1%), 2,388 patients (mean age (SD) 76.9 (12.7) years; 47.3% men, 87% ischaemic stroke) were included in the study.

Table 1. Sample characteristics on admission, and their independent association with 1-year mortality in Anglia Stroke Clinical Network Evaluation Study (2009–12)

Patients' characteristic	Total (N = 238,888)	%	Death (N = 759)	% Who died	OR[a]	95% CI[a]	P[a]
Age quintiles (years)							<0.001[b]
18–64	463	19.4	54	11.7	1.0	–	
65–75	434	18.2	85	20.0	1.5	1.0–2.2	0.028
76–81	491	20.6	133	27.1	2.3	1.7–3.1	<0.001
82–86	452	19.0	187	41.4	3.8	2.5–5.6	<0.001
87–101	544	22.8	298	54.8	6.1	3.5–10.4	<0.001
Sex							
Female	1,256	52.6	454	36.2	1.0	–	
Male	1,130	47.4	305	27.0	1.2	0.8–1.6	0.36
Type of stroke							<0.001[b]
Infarct	1,990	86.8	569	29.6	1.0	–	
Haemorrhage	288	12.6	147	51.0	2.3	1.5–3.6	<0.001
Haemorrhagic infarct	16	0.70	5	31.3	0.7	0.2–2.8	0.65
OCSP classification							<0.001[b]
PACS	825	39.6	184	22.3	1.0	–	
LACS	517	24.8	78	15.1	0.8	0.5–1.1	0.20
POCS	295	14.1	68	23.1	1.4	1.0–2.1	0.06
TACS	449	21.5	315	70.2	7.4	5.9–9.3	<0.001
Prestroke mRS							<0.001[b]
0	959	50.0	163	17.0	1.0	–	
1	360	18.8	110	30.6	1.8	1.3–2.4	<0.001
2	206	10.7	74	36.0	2.4	1.6–3.6	<0.001
3	208	10.8	109	52.4	4.3	2.9–6.4	<0.001
4	131	6.8	88	67.2	6.5	4.3–10.0	<0.001
5	55	2.9	43	78.2	8.9	3.8–21.2	<0.001
Glucose quintile (mmol/L)							<0.001[b]
<5.6	386	18.7	97	25.1	1.0	–	
5.7–6.4	428	20.7	107	25.0	0.9	0.6–1.3	0.47
6.5–7.3	418	20.3	106	25.4	1.0	0.7–1.3	0.86
7.4–8.9	409	19.8	151	36.9	1.5	1.1–2.0	0.02
>8.9	423	20.5	199	47.0	1.9	1.4–2.5	<0.001
Ischaemic heart disease							
No	1,700	75.1	517	30.4	1.0	–	
Yes	565	24.9	220	38.9	1.3	1.1–1.6	0.01
Diabetes							
No	1,889	83.0	607	32.1	1.0	–	
Yes	388	17.0	135	34.8	0.9	0.6–1.3	0.52
Hypertension							
No	949	41.7	316	33.3	1.0	–	
Yes	1,329	58.3	426	32.1	0.8	0.7–1.0	0.02

[a]Multiple logistic regression model, adjusted for all other variables in the table and for intra-hospital correlation of outcome, after multiple imputation of missing covariate data. Pseudo R2 for complete case analysis = 0.29.

[b]Wald test for all categories of variable. PACS, partial anterior circulation stroke; LACS, lacunar stroke; OCSP, Oxfordshire Community Stroke Project; POCS, posterior circulation stroke; TACS, total anterior circulation stroke.

Table 1 shows the distribution of the sample characteristics with regard to demographics, stroke-related factors (subtype, severity taken as reflected by Oxfordshire Community Stroke Project (OCSP) type), prestroke disability as modified Rankin score (mRS) and major cardiovascular co-morbidities. The total sample characteristics and the sample characteristics of those who died within 1 year or not (primary outcome) are presented separately. Table 1 also shows the multiple logistic regression model results adjusted for all patient-related characteristics shown in the table and for intra-hospital correlation of outcome, after multiple imputation of missing covariate data. Increasing age, haemorrhagic stroke type, total anterior circulation stroke, increasing prestroke frailty depicted by mRS, higher glucose level on admission, history of ischaemic heart disease and hypertension were identified as patient level prognostic factors that were independently associated with significant effect on mortality at 1 year. These prognostic variables explained 29% of the variance in 1 year mortality (pseudo $R^2 = 0.29$). For the equivalent logistic regression models with 7-day and 30-day mortality as outcomes, the pseudo R^2 values were 0.31 and 0.32, respectively. For the equivalent Cox model, the R^2 value was 0.62 (data not shown).

Supplementary Table 1, available at *Age and Ageing* online shows the characteristics of each stroke unit and their mortality rates at 7 and 30 days and 1 year after admission stroke event. There was wide variation in characteristics of services but there were no obvious outliers.

Table 2 shows the associations between the selected stroke unit characteristics and odds of mortality for the three time points, as well as hazards of death during 1 year of follow-up, adjusted for patient's prognostic factors. Overall all service characteristics indicative of a better resourced unit, that is, with higher staffing levels, were associated with better outcomes across these time points. Type of hospital (district general or university) and ratio of stroke admissions per bed per month were less consistently associated with lower mortality. Having an early supported discharge service was not associated with a reduction in mortality but higher trained nursing staff levels were consistently associated with decreased death rates.

Table 3 shows the stroke unit characteristics independently associated with each outcome after mutual adjustment for other influential hospital characteristics. A consistent finding was that higher trained nurse (NHS staff grade 5 and above, i.e. staff nurse or senior staff nurse) to bed ratios were associated with lower all-cause mortality. In addition, more beds per stroke unit and fewer admissions per bed per month were independently associated with higher mortality within a year and not having an early discharge policy were also associated with greater odds of death within 7 days. Fewer beds per stroke unit, more rehabilitation beds, not having an early discharge policy and being in a university hospital were associated with higher odds of death within 30 days. Complete case analyses without imputed data produced similar results.

Discussion

In this study, we found that whilst there was considerable variations in stroke service provision amongst the stroke units even within a relatively small geographical region, variation in mortality outcomes following acute stroke was not significantly different, if unadjusted data were used. Stroke mortality, however, appeared to be strongly influenced by certain known patient level characteristics and certain service characteristics. Higher nursing:beds ratio was strongly and consistently associated with a better mortality outcome even after controlling for patient level prognostic factors. These results suggest that increasing stroke unit staff by one whole time equivalent trained nurse for every 10 beds could reduce 1 year mortality significantly by 8–12% (Table 3).

Some of these findings, however, require cautious interpretation as they may be partly explained by confounding factors that are not adequately adjusted for e.g. more severe cases being admitted to larger units with neurosurgical facility. Larger units are not necessarily equipped with better resources; indeed as evident in our study many indicators of better resources are associated with a lower mortality (see Table 2). This study has focused on type of services/staffing and outcome relationship rather than process

Table 2. Associations between mortality at various time points and single stroke unit characteristics, adjusted for patients' prognostic characteristics on admission

Outcome	Time to death[a]			Died within 7 days[b]			Died within 30 days[b]			Died within 365 days[b]		
Stroke unit characteristic	Hazard ratio	95% CI	*P*	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*
District general vs university hospital	0.91	0.70–1.18	0.474	0.80	0.58–1.11	0.181	0.69	0.52–0.93	0.013	0.89	0.61–1.31	0.568
Early supported discharge service	1.27	1.08–1.49	0.003	1.28	0.95–1.71	0.099	1.41	1.04–1.91	0.029	1.40	1.04–1.88	0.028
No. of stroke admissions per month (per 10 beds)	1.04	1.00–1.07	0.037	1.07	1.01–1.12	0.017	1.07	1.03–1.13	0.001	1.07	1.02–1.11	0.003
No. of stroke unit beds (per 10 admissions)	1.09	1.05–1.13	<0.001	1.14	1.05–1.24	0.001	1.21	1.12–1.29	<0.001	1.13	1.07–1.21	<0.001
Ratio stroke admissions per month: stroke unit beds	0.92	0.64–1.31	0.166	1.07	0.62–1.86	0.809	0.89	0.47–1.66	0.694	1.09	0.65–1.83	0.747
No. of rehabilitation beds in unit (per 10 beds)	1.09	0.96–1.23	<0.001	1.17	1.01–1.36	0.036	1.23	1.05–1.44	0.010	1.08	0.90–1.28	0.418
Staff: bed ratios (No. of staff per 10 stroke unit beds)												
Trained nurses[c]	0.94	0.91–0.96	<0.001	0.94	0.89–0.99	0.018	0.93	0.86–0.99	0.032	0.90	0.88–0.92	<0.001
Stroke consultants	0.65	0.47–0.89	0.007	0.93	0.51–1.71	0.826	0.54	0.29–1.02	0.058	0.56	0.38–0.82	0.003

Each hazard ratio is from a separate regression model. All regression models adjusted for age, type of stroke, OCSP classification, modified Rankin score, ischaemic heart disease, hypertension, blood glucose level on admission; not mutually adjusted for the other stroke unit characteristics.

[a]Cox regression models, censored at 365 days.

[b]Logistic regression models.

[c]NHS Band 5 and above (bands 5, 6 and 7).

Table 3. Associations between mortality outcomes and mutually adjusted stroke unit characteristics, also adjusted for prognostic characteristics on admission

Outcome	Time to death[a]			Died within 7 days[b]			Died within 30 days[b]			Died within 365 days[b]		
Stroke unit characteristic	Hazard Ratio	95% CI	*P*	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*	Odds ratio	95% CI	*P*
District general vs university hospital							0.62	0.49–0.79	<0.001			
Early stage discharge policy during study				0.48	0.29–0.82	0.007	0.50	0.28–0.89	0.018			
No. of stroke unit beds (per 10 beds)	1.07	1.03–1.12	0.003	1.41	1.17–1.71	<0.001	0.86	0.74–0.99	0.042			
No. of rehabilitation beds in unit (per 10 beds)							1.24	1.02–1.50	0.028			
Ratio stroke admissions per month: stroke unit beds	0.84	0.74–0.96	0.010									
No. of nurses per 10 stroke unit beds	0.94	0.92–0.95	<0.001	0.74	0.75–0.94	0.002	0.80	0.72–0.89	<0.001	0.90	0.88–0.92	<0.001
R^2 for model[c]	0.62			0.31			0.33			0.30		

Each column of hazard ratios is from the same multiple regression model. All regression models adjusted for age, type of stroke, OCSP classification, modified Rankin score, ischaemic heart disease, hypertension, blood glucose level on admission; not mutually adjusted for the other stroke unit characteristics not listed in the table.

[a]Cox regression model, censored at 365 days.

[b]Logistic regression models.

[c]Royston R^2 for Cox model, pseudo R^2 for logistic regression models. Only nurses:bed as the service characteristic in 'Died within 365 days' model.

measures and outcome. Care processes after admission are not confounders but intermediate variables that lie on casual pathways between prognostic characteristics and outcomes, therefore in principle they should not be adjusted for in regression models such as ours.

Higher nursing staffing levels are consistently associated with mortality outcomes at all time points up to 1 year, independently of other factors and controlling for individual level prognostic indicators. Nursing staffing levels have been previously shown to be linked to patient outcome in general patient population as well as in stroke [21, 22]. Bray *et al.* [22] examined the effect of nursing staff ratios on 30-day mortality in stroke patients admitted to stroke units participating in the Stroke Improvement National Audit Programme in the United Kingdom. They showed higher ratio of number of nursing staff:10 bed was associated with significantly reduced 30-day post stroke mortality. Cho *et al.* [23] showed stronger effect size with reduced odds of 30-day mortality in both general ward and ITU setting. The current study has furthered this knowledge and provides new evidence that higher trained nursing staffing levels are associated with better mortality outcome up to 1 year post stroke.

There is growing evidence of the impact that the National Stroke Strategy and SSNAP audits have had on stroke care provision particularly around processes and outcomes over last 10 years. Our study has added to this evidence by providing further information with regard to service level characteristics that are important to deliver optimal process and quality of care given to people with stroke. The major strength of our study is its prospective design to specifically address the research questions [13]. There was wide variation in stroke unit characteristics that reflects the variety of the UK stroke units in the NHS setting (Supplementary Table 1, available at *Age and Ageing* online). All stroke cases were vetted by specialist teams and prospectively identified. Data collection was standardised across the sites and robust statistical methods are employed to impute missing data.

There are some limitations. We have relatively few sites, and some site characteristics (such as neurosurgery facility) were restricted to one or two sites while others were correlated with each other. It is thus possible that some of the hospital characteristics included in the final regression models might actually have indirectly reflected other characteristics of the same hospitals. These results should therefore be interpreted with caution. Nonetheless, our findings do show that staffing level and manageable unit size with less pressure on beds are the characteristics of services that are consistently associated with lower mortality. We are unable to control for acute stroke severity measure such as NIHSS, but we have controlled for OSCP classification which is a good prognosis marker for both acute and longer term mortality outcome.

While centralisation of services has happened in settings with clear benefits has been shown in densely populated regions such as London and Manchester in United Kingdom [24, 25], the impact of such centralisation in rural areas has yet to be examined. There are concerns of centralisation in rural areas such as Anglia region due to travel times for thrombolysis. Our study provides robust evidence that even in rural areas if stroke units were equipped with optimal staffing mortality outcome can be improved. Indeed, Fulop *et al.* [26] recently highlighted challenges in evaluation of health system changes due to the different timings of the reconfigurations; the retrospective nature of the evaluations; and the current organisational turbulence in the English NHS.

The UK NHS system is health care model as a universal free at the point of care health care system, which has been shown to be very cost efficient [27]. Our results highlight the importance of staffing levels and having a reasonable catchment population/stroke service as key factors associated with a better mortality outcome in stroke, which is one of the biggest killers globally. Our study thus provides useful information to local populations, clinicians and service providers across the world to design stroke services that would address these key determinants of stroke mortality outcome.

Key points

- Variation in stroke services explained very little of the variation in mortality in stroke.
- Patient level prognostic variables explained 29% of the variance in 1-year mortality in stroke.
- Every 1 point increase in trained nurses per 10 beds was associated with significant reduction in stroke mortality.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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Authors' contributions

P.K.M., D.J.D. and M.O.B. conceived the idea. P.K.M. is the PI of the ASCNES study. J.F.P., M.O.B., A.K.M., G.M.P. and E.A.W. are co-applicants of the grant and co-investigators of the ASCNES. D.J.D. is study steering committee member. R.H. developed electronic data collection forms with PKM and collected data at one site and provided secretarial support. S.D.M. coordinated the study and managed and cleaned the data with G.M.P. M.O.B. and G.M.P. performed the statistical analyses. P.K.M., M.O.B. and Y.K.L. drafted the manuscript and all co-authors contributed in the writing of the paper.

Conflicts of interest

None declared.

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Ethical approval

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