

# Upgraded Acute Stroke Care Including Thrombolysis Is Associated with Reduced Length of Hospital Stay among Non-Stroke Patients

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## Key Words

Acute stroke · Length of hospitalization · Thrombolysis · Imaging

## Abstract

**Background:** Implementing thrombolytic therapy in a stroke unit (SU) profoundly affects the resources available to all patients admitted for suspected acute stroke. We examined the benefits of an acute stroke service to non-stroke patients in terms of length of hospitalization, and estimated the economic impact in terms of derived costs. **Methods:** We performed a historical follow-up study of 792 non-stroke patients admitted to our SU for suspected stroke before, during and after implementing thrombolysis as part of our service. Data on demographic and clinical characteristics, including imaging data and final diagnoses, and length of stay (LOS) were collected prospectively. Multivariate logistic regression analysis was performed to identify variables associated with LOS. **Results:** Median LOS for non-stroke patients in the SU decreased from 43.8 h (interquartile range, 19–96) to 23.5 h (16–44) after implementing thrombolytic therapy. Total hospital LOS for non-stroke patients decreased from 52.7 (22–147) to 28.7 (21–124) h during the same period. Initial magnetic resonance imaging was associated with shorter LOS in the SU. The derived cost reductions from shorter LOS reduced the costs of implementing recombinant tissue plas-

minogen activator treatment. **Conclusions:** Stroke care reorganization following the introduction of thrombolytic treatment was associated with a 50% reduction in LOS for non-stroke patients admitted to the SU. Reduced LOS in the SU for non-stroke patients could further add to the cost-effectiveness of thrombolytic treatment.

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## Introduction

The introduction of stroke units (SU) and the implementation of intravenous recombinant tissue plasminogen activator treatment (alteplase; rtPA) has improved the prognosis and functional outcome for stroke victims [1, 2]. All patients with confirmed stroke diagnosis benefit from the specialized stroke management and care, although only 1–10% of all stroke patients are offered rtPA. The use of thrombolytic treatment in specialized units has proven to be cost-effective for stroke patients [3, 4]. Costly organizational changes with stroke codes, ‘fast tracks’ and rapid access to neuroimaging may also benefit the large number of patients referred for suspected stroke, but who are subsequently discharged with other diagnoses, in terms of faster and more efficient diagnosis and management. This patient group comprises 15–40% of patients evaluated for acute stroke [5–7]. The improved

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management of these patients could provide an important derived benefit when evaluating the cost-effectiveness of thrombolytic treatment.

For stroke patients, studies have demonstrated that rapid diagnostic work-up with immediate computed tomography (CT) is cost-effective [8]. Although the costs of neuroimaging are high, these costs are outweighed by a reduced length of stay (LOS) in the hospital, because efficient management and better outcomes depend on accurate early diagnosis. LOS is highly predictive of total inpatient costs of hospitalization [9–11].

In patients with transient ischemic attacks (TIA) and other patients who are subsequently diagnosed as non-strokes, LOS could be influenced greatly by rapid diagnostic protocols and qualified medical evaluation [12]; however, to our knowledge, there are no published data on the predictors of LOS for non-stroke patients admitted to SU.

This study evaluates changes in LOS and related hospitalization costs for non-stroke patients that coincided with improved stroke services, including the implementation of acute thrombolytic therapy, in our SU. Furthermore, we identified predictors of LOS for this patient group.

## Methods

The study is a historical follow-up of all patients admitted to our SU between 1 January 2003 and 31 December 2006 under suspicion of acute stroke, who were subsequently discharged with diagnoses other than stroke or TIA. During this period, the SU evolved from being inexperienced with thrombolysis (until April 2004) to having implemented 24-hour magnetic resonance imaging (MRI)-based rtPA treatment (by April 2006), treating almost 10% of ischemic stroke patients in our service area by December 2006.

We evaluated changes in LOS relative to the 2-step introduction of rtPA therapy described below.

### *Organization of Stroke Service*

The protocol for acute stroke care in our institution was as follows, depending on whether care was provided before, during or after the introduction of thrombolytic treatment:

*Stage I.* Until 1 April 2004, the SU of the Department of Neurology, Aarhus University Hospital, consisted of 10 beds, served a population of 130,000 inhabitants, and provided diagnostic and initial rehabilitative care for stroke patients according to national stroke guidelines [13]. Patients were referred to the SU from the emergency room (ER), from other hospitals, directly from the emergency services or from primary care physicians. Patients were discharged from the SU to other (non-neurological) hospital departments for further specific treatment, to their home or to a rehabilitation facility.

*Stage II.* Between 1 April 2004 and 31 March 2006, MRI-based rtPA was administered to patients admitted directly to the SU between 8:00 a.m. and 4:00 p.m., weekdays. Patient referral, evaluation, neuroimaging, rtPA treatment and care were provided by a small team of specialized nurses and physicians. Other organizational changes included a fast-track system that allowed direct admission of patients with presumed stroke from the emergency services and general practitioners, and a 'stroke code' by which the stroke team could be contacted.

*Stage III.* From 1 April 2006, MRI-based rtPA was administered on a 24-hour, 365-day basis. Beginning on 1 January 2006, the number of SU beds increased from 10 to 17 in order to accommodate an extended uptake area of 300,000 inhabitants for all types of stroke and 600,000 inhabitants for acute stroke (within 0–3 h of onset).

### *Patient Selection*

Study inclusion criteria were hospitalization in our SU between 1 January 2003 and 31 December 2006 under suspicion of acute stroke. Patients were admitted to the stroke unit if the reported symptoms were judged to be of cerebrovascular origin by the neurologist on call, at the telephonic preadmission assessment and otherwise to the general neurological ward. Exclusion criteria were discharge diagnosis of acute stroke according to the International Classification of Diseases version 10 (ICD-10: I60–I64) and TIA (G45.0–G45.9) [14]. Admissions due to sequelae from a previous stroke (I69) were registered as non-strokes and were included in the study.

### *Possible Predictors of LOS*

All patients referred to the SU received a neurological evaluation that included a Scandinavian Stroke Scale score (SSS), which reflects the severity of stroke symptoms and ranges from 0 to 58 (58 equals no symptoms) [15].

Data on possible predictors of LOS were registered prospectively, and included age, sex, SSS on admission, exact times of admission, referral to SU, discharge from SU and discharge from hospital, as well as exact times of neuroimaging and choice of imaging modality (CT or MRI). Final diagnoses were coded by the attending SU physician. Diagnoses were subsequently grouped according to ICD-10 chapters [14]. The non-specific diagnosis groups Z (factors influencing health status and contact with health services) and R (symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified) were merged, and diagnosis groups with less than 5% of patients were merged and classified as 'others'.

### *Length of Stay and Imaging Delay*

LOS at the SU and total hospital LOS were calculated from the registered admission, transfer and discharge data. Total hospitalization time included additional stay at any other hospital unit before or after the stay at the SU. For patients admitted from or referred to other hospitals, the hospital discharge registry includes dates, but not exact times for first admission or final discharge. Data on exact time of first admission were missing for 30 patients; therefore, these patients were assigned the earliest possible time on that date (12:00 a.m.). Data on exact time of discharge were missing for 44 patients; therefore, these patients were assigned the latest possible time on the date (11:59 p.m.). Patients with missing time data were evenly distributed throughout the 3

**Table 1.** Demographics and time delays for non-stroke patients in the SU

	Stage I (n = 160)	Stage II (n = 411)	Stage III (n = 221)	Total (n = 792)
Age, years	54 (40–67)	55 (42–68)	60 (45–76)	56 (42–69)
Male gender, n	94 (59)	219 (53)	112 (51)	425 (54)
SSS	56 (46–58)	56 (48–58)	55 (46–58)	56 (46–58)
Discharge diagnosis (ICD-10) chapter				
F	5 (3)	37 (9)	19 (9)	61 (8)
G	39 (24)	120 (29)	59 (27)	218 (28)
H	10 (6)	35 (9)	14 (6)	59 (7)
I	20 (12)	42 (10)	29 (13)	91 (11)
R and Z	68 (42)	101 (25)	60 (27)	229 (33)
Other	18 (11)	76 (18)	40 (18)	134 (17)
Neuroimaging				
No imaging	17 (11)	46 (11)	19 (9)	82 (10)
CT	123 (77)	291 (71)	163 (74)	577 (73)
MRI	20 (12)	74 (18)	39 (18)	133 (17)
Imaging delay, h <sup>1</sup>	5 (2.1–16)	3.3 (1.3–10.5)	3.2 (1.4–6.3)	3.75 (1.7–10)
LOS (SU), h	43.8 (19–96)	24.7 (16–64)	23.5 (16–44)	25.2 (17–66)
LOS (total hospital), h	52.7 (22–147)	43.7 (21–139)	28.7 (19–97)	41 (21–124)

Data are presented as medians with interquartile ranges in parentheses or numerals with percentages in parentheses.

ICD-10 groups: F = Mental and behavioral disorders; G = diseases of the nervous system; H = eye and ear diseases; I = diseases of the circulatory system; R = symptoms and abnormal findings not classified elsewhere; Z = factors influencing health status and contacts with health services.

<sup>1</sup> Calculated from first hospital admission to first imaging study.

organizational stages. Stays at rehabilitation facilities were not included in the LOS. If the patient died during hospitalization, the time of discharge was substituted with the time of death.

Imaging delay was calculated as the period from the time of primary admission to either hospital or SU until the time of imaging. The cumulative proportion of patients undergoing imaging was calculated as a function of time.

#### Statistical Analysis

Comparison of patient characteristics, use of CT/MRI and LOS between the 3 organizational stages was performed using ANOVA and/or Student's *t* test and  $\chi^2$  test. Multiple linear regression analysis was employed to examine possible predictors of SU and total LOS, including organizational stage (stage I, II or III), imaging (none, CT, MRI) and patient characteristics (age, gender, living arrangements, SSS and diagnosis) as covariates. SU and total LOS were log-transformed because they did not follow a Gaussian distribution according to Wilk-Shapiro/Rankit plots. Therefore, the comparisons of LOS reflect the ratio of median LOS before and after full implementation of thrombolytic treatment. All analyses were performed using R version 2.4.1.

#### Cost Analysis

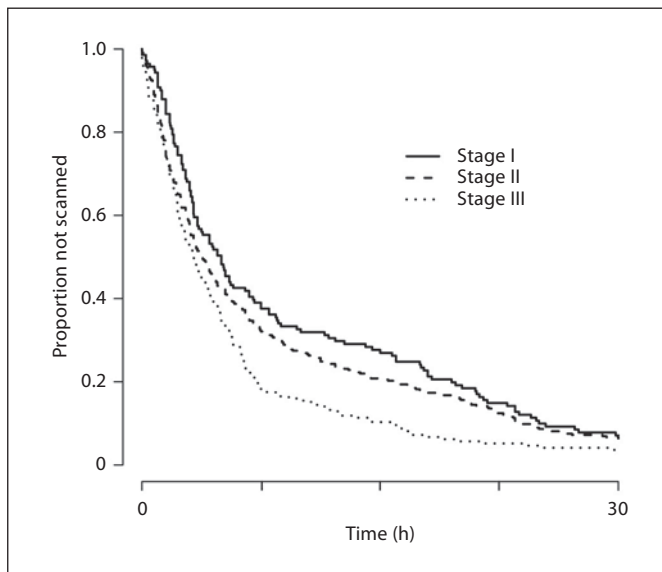
The economic impact of the organizational changes was calculated as the savings in bed time costs for non-stroke patients. The reduced LOS per patient (hours per average non-stroke patient admitted to the SU) was calculated as the difference in the

geometric mean between stage I and stage III for the SU and total hospital LOS. The total annual reduction in SU and total hospital LOS was calculated by multiplying these per patient LOS ('avoided' bed time) by the 2006 admission number. The total savings was calculated by multiplying the reduced LOS with the price of a bed-day at the SU at Aarhus University hospital (prices 2006). As a measure of the uncertainty of cost estimates, the upper and lower value of the confidence interval (CI) from the multivariate regression analysis was used.

## Results

Eight hundred and twenty patients were included in the database during the 4-year period; 168 patients were registered in stage I, 426 in stage II and 226 in stage III. Twenty-eight patients were excluded from further analysis due to incomplete data (*n* = 10) or accidental registration of patients with a stroke discharge diagnosis (*n* = 18).

The admission rate was 10.7 patients per month during stage I, 17.1 patients per month during stage II, and 24.6 patients per month during stage III, reflecting the increase in admissions.



**Fig. 1.** The cumulative proportion of patients not yet scanned according to organizational stage.

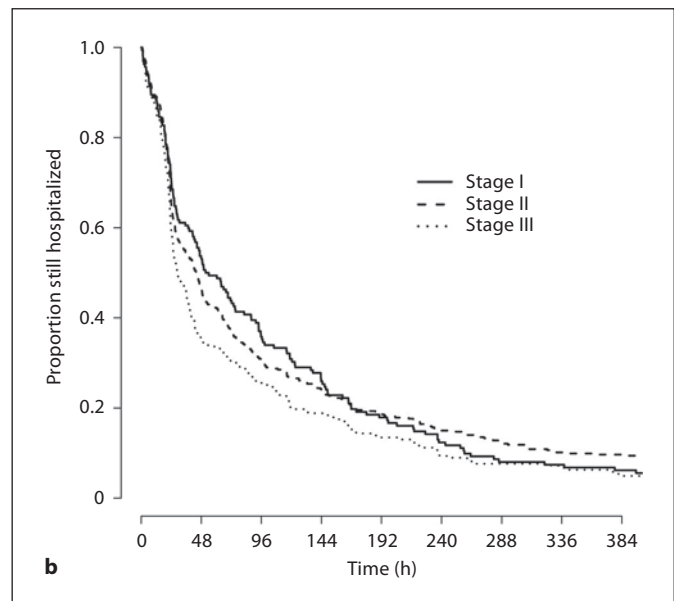
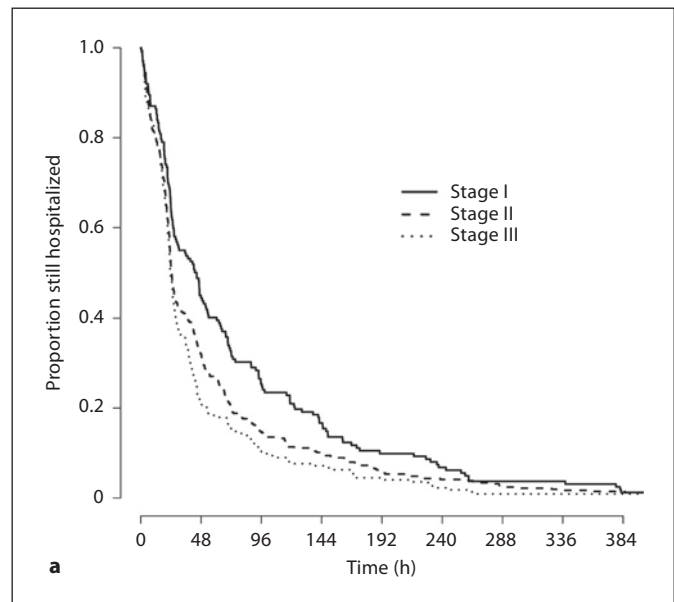
During the same periods, the numbers of patients registered with stroke diagnoses (ICD-10: I61, I63–I64) were 257 (average 17.1 patients/month) in stage I, 588 (24.5 patients/month) in stage II, and 487 (54.1 patients/month) in stage III.

Table 1 shows the demographic characteristics, SSS, discharge diagnosis, imaging modality and LOS for the 792 patients.

#### Imaging

Most patients (90%) received neuroimaging during hospitalization. CT was the primary imaging modality for 77% of patients and MRI for 17%. MRI was used more frequently during stage III (full implementation of MRI-based thrombolysis) than during stage I (18 vs. 12%, respectively). One hundred and six patients (14%) underwent additional secondary imaging during hospitalization; 96 of 577 patients (17%) who underwent CT as the primary imaging modality received an MRI with a median delay of 50.5 h. For 5 patients, primary MRI was followed by a secondary CT scan.

Imaging delays were reduced with the implementation of thrombolytic treatment (fig. 1), despite increased patient flow. The proportions of patients imaged within 6 h were 54% in stage I, 57% in stage II and 65% in stage III. Imaging was performed within 12 h in 64% during stage I, 69% during stage II and 81% during stage III.



**Fig. 2.** The proportion of patients who remained hospitalized in the SU (a) and hospitalized in general (b) according to organizational stage.

#### Stroke Unit Length of Stay

There was a significant decrease in median LOS for non-stroke patients over time (fig. 2a). Median LOS in the SU was reduced from 43.8 h in stage I to 24.7 h in stage II ( $p < 0.005$ ), and was further reduced to 23.5 h in stage III ( $p < 0.005$ ). When we compared data from the 3 organizational stages in a multivariate linear regression mod-



**Table 2.** Possible predictors of LOS in the SU and of total hospitalization time

	Adjusted relative median			
	LOS (SU)	CI	LOS (total hospitalization)	CI
Time period				
Stage I	1.00	reference	1.00	reference
Stage II	0.72	0.58–0.90	0.91	0.72–1.15
Stage III	0.59	0.46–0.75	0.62	0.48–0.81
Age	1.04	0.99–1.09	1.10	1.04–1.16
Sex				
Male	1.00	reference	1.00	reference
Female	0.87	0.74–1.03	0.95	0.80–1.14
SSS	0.92	0.84–1.0	0.78	0.71–0.86
Discharge diagnosis				
R and Z	1.00	reference	1.00	reference
F	1.25	0.89–1.76	1.04	0.73–1.50
G	1.08	0.87–1.35	1.20	0.95–1.52
H	1.22	0.87–1.71	1.13	0.78–1.62
I	1.49	1.12–1.99	1.81	1.33–2.47
Other	1.16	0.89–1.50	2.33	1.77–3.08
Neuroimaging				
CT	1.00	reference	1.00	reference
No imaging	0.25	0.19–0.33	0.31	0.23–0.41
MRI	0.64	0.51–0.81	0.89	0.69–1.14

ICD-10 groups: F = Mental and behavioral disorders; G = diseases of the nervous system; H = eye and ear diseases; I = diseases of the circulatory system; R = symptoms and abnormal findings not classified elsewhere; Z = factors influencing health status and contact with health services.

el, LOS in the SU remained substantially lower in stages II (adjusted relative median LOS = 0.72; 95% CI, 0.58–0.90) and III (adjusted relative median LOS = 0.59; 95% CI, 0.46–0.75) compared to stage I. Factors (other than stage) associated with a shorter LOS in the SU included use of MRI, no imaging (when compared with the use of CT) and a cardiovascular or ‘other’ discharge diagnosis (table 2).

#### *Total Length of Hospitalization*

The total hospital LOS decreased from 52.7 h in stage I to 43.7 h in stage II and 28.7 h in Stage III (fig. 2b). The drop in LOS from stage II to III was significant ( $p < 0.0005$ ).

The adjusted relative median total LOS in stages II and III were 0.91 (95% CI, 0.72–1.15) and 0.62 (95% CI, 0.48–0.81), respectively. Factors associated with a shorter total LOS were: high SSS score and no imaging (vs. CT), whereas higher age and a cardiovascular or ‘other’ discharge

diagnosis were associated with a longer total LOS (see table 2). For comparison, the hospital patient registry showed a general trend of LOS reduction for all patients from 108 to 98 h (9%) during the same period.

#### *Costs*

Table 3 shows the estimated savings in bed time costs for non-stroke patients concurrent with the organizational changes related to the implementation of centralized rtPA treatment. We calculated the economic savings (roughly USD 220,192; table 3) based on our 2006 patient intake ( $n = 338$ ) and the difference between the geometric means of LOS for stage I and stage III (14.8 h for SU LOS and 13.9 h for total hospital LOS).

#### **Discussion**

This study reports changes in the LOS in SU for non-stroke patients. The analysis demonstrates that a substantial reduction in LOS coincided with the organizational changes in acute stroke care (stroke code, fast track, thrombolysis, acute neuroimaging) at our hospital. While both stroke and non-stroke patients outnumber patients who eventually receive rtPA, our study demonstrates that even non-stroke patients benefit from the improved stroke service in terms of faster imaging, faster diagnosis and shorter LOS.

We found a reduction in median LOS for non-stroke patients from 43.8 h to 23.5 h, corresponding to a reduction of 46% in 4 years. This reduction is much larger than the general reduction in average LOS for the hospital during the same period (9%). The general trend towards shorter LOS is driven by financial pressure on hospital budgets and a continuous demand for increased productivity. However, reductions in LOS do not happen by themselves, they are facilitated by the implementation of new technologies, organizational changes and management attention. Our data show that implementing an improved stroke service can improve productivity during the treatment of stroke and non-stroke patients.

From the perspective of health care providers, these data offer insight into indirect benefits derived from what might appear to be a costly infrastructure to support acute rtPA treatment. Previous economic analysis from our center estimated that the additional cost of the organization in phase III corresponded to USD 5,978 per patient receiving rtPA, or double the price of conventional treatment (as in stage I) [3]. In 2006, 87 patients received rtPA in our SU, at an estimated additional cost of USD

**Table 3.** Savings in bed time costs for non-stroke patients in the SU, Aarhus University Hospital (based on 2006 figures)

	Reduced LOS per patient, h	Reduced LOS for all non-stroke patients, h	Savings and CI, USD per patient	Total savings and CI, USD per year
SU	14.8	4,997	692 (432–972)	233,737 (146,035–328,578)
Total hospitalization	13.9	4,707	652 (457–1,252)	220,192 (154,629–422,826)

520,086. Although the aforementioned analysis showed that thrombolysis is cost-effective based on the benefit to rtPA-treated patients alone, the indirect savings by shorter LOS during the same period (USD 220,192; table 3) also partly counterbalances the expense associated with implementing acute thrombolytic therapy. Cost analysis suggests that a fast track and acute neuroimaging for presumed acute stroke has an economic value for patients other than those eligible for thrombolysis treatment. This benefit is generally not accounted for in cost-effect analysis of thrombolysis treatment for acute ischemic stroke [3]. We believe the savings calculated according to our analysis represents a conservative estimate. Theoretically, the real cost to society of a given resource is its opportunity cost, the value of the resource in its next best alternative use [16]. In this case, extra funding was needed to carry through the organizational changes in stages II and III, and the marginal cost of a bed-day in the new fast track for presumed acute stroke is higher than the average price of a bed-day in the SU [3]. To reflect this, the price of a bed-day used in our calculations should have been adjusted upwards. However, because it is difficult to calculate a precise opportunity cost for bed time, we used the hospital's 2006 price for a bed-day in the SU. It should be noted that this price includes the total average cost (variable and fixed costs) without profit.

LOS in the SU was related to neuroimaging. Patients who did not undergo neuroimaging had a shorter LOS. We ascribe this to clinical findings that prompted fast discharge rather than further diagnostics. Primary MRI was also associated with a shorter LOS compared to CT. MRI is more sensitive and specific to cerebral ischemia than CT is [6], which could facilitate diagnostic evaluation and medical decision-making. The larger proportion of patients imaged by MRI and within 12 h of hospitalization during stage III is likely to be an important contributing factor to the LOS reduction.

The SU at our hospital is organized somewhat differently than many other stroke services. Patients are admitted directly to the SU from the emergency services, general practitioners and ER from other hospitals in a coun-

ty of 600,000 inhabitants. It could be argued that the more common referral pattern, where admitted patients are screened in the ER, represents a more efficient use of resources in a highly specialized SU. However, our experience shows that direct referral to the SU with centralized rtPA treatment is efficient, and has provided rtPA treatment to 10% of all ischemic stroke patients in our area. We have shown that this organization is efficient from both quality and economic perspectives [3], and argue that the indirect benefits for managing patients who receive other diagnoses than stroke further emphasize the benefits of rapid neurological evaluation and MRI for patients with suspected stroke.

Our study has several limitations. Firstly, the general tendency for patient care to become more efficient with time contributes to shorter LOS over time, and could account for the reduced LOS that we observed. This general reduction in LOS at the hospital accounted for 9% suggesting that the effect of organizational changes was larger by far than the general tendency toward reduced LOS. In addition, the improvements were observed despite a doubling of patient intake.

Secondly, our approach did not permit us to establish any causal link between specific diagnoses or diagnostic approaches and reduced LOS. Furthermore, the merging of diagnoses into larger groups could obscure specific information regarding the impact in certain subgroups. Diagnoses were assigned by the stroke physician attending the SU, but no follow-up or evaluation was performed to ensure correctness. This study does not address patient satisfaction or potential disadvantages associated with reduced LOS.

In our economic analysis based on results from a single center, estimated savings due to reduced LOS might not apply to non-stroke patients in any SU setting. The exact savings depend on a number of factors not included in this study. The reduction in LOS that we observed is only possible with access to bed time assigned to high-quality treatment, specialized nurses, 24-hour in-house neurology coverage and access to prompt imaging. Therefore, an increase in the average cost per hour might offset

the savings of the reduced LOS. Ideally, a full cost-effectiveness analysis that compares both costs and effects of treating non-stroke patients in a fast track for presumed acute stroke and a 'non-acute' track should be performed.

This study did not investigate variables other than LOS to characterize changes in quality of patient management and care. However, this limitation is inherently difficult to overcome in a group of patients with very heterogeneous disease patterns.

## Conclusion

Upgraded acute stroke service with thrombolytic therapy can lead to more rapid diagnostic imaging and reduced LOS and hospitalization costs for patients ultimately discharged with a non-stroke diagnosis.

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