Impact of ongoing centralization of acute stroke care from "drip and ship" into "direct-to-mothership" model in a Dutch urban area

Linden, M.C. van der; Linden, N. van der; Lam, R.C.; Stap, P.; Brand, C.L. van den; Vermeulen, T.; ... ; Wijngaard, I.R. van den

Health policy 125 (2021) 1040–1046

Contents lists available at ScienceDirect

Health policy

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

Impact of ongoing centralization of acute stroke care from “drip and ship” into “direct-to-mothership” model in a Dutch urban area

M. Christien VAN DER LINDEN[a,1,*], Naomi VAN DER LINDEN[b,1], Rianne C. LAM[c], Peter STAP[d], Crispijn L. VAN DEN BRAND[e], Tamara VERMEULEN[f], Korné JELLEMA[g], Ido R. VAN DEN WIJNGAARD[h]

[a] Clinical Epidemiologist, Haaglanden Medical Centre (HMC), P.O. Box 432, 2501 CK The Hague, the Netherlands
[b] Assistant Professor, Department of Health Technology and Services Research, Technical Medical Centre, University of Twente, P.O. Box 217, 7500 AE Enschede, the Netherlands
[c] Emergency Nurse Practitioner, Emergency Department, HMC, P.O. Box 432, 2501 CK The Hague, the Netherlands
[d] Emergency Nurse Practitioner, Emergency Department, HMC, P.O. Box 432, 2501 CK The Hague, the Netherlands
[e] Emergency Physician, HMC and Scientific Lead at Dutch Institute for Clinical Auditing, P.O. Box 432, 2501 CK The Hague, the Netherlands
[f] Nurse Practitioner Neurology, Department of Neurology, HMC, P.O.Box 432, 2501 CK The Hague, the Netherlands
[g] Neurologist, Department of Neurology, HMC, P.O. Box 432, 2501 CK The Hague, the Netherlands
[h] Neurologist, Department of Neurology, HMC, P.O. Box 432, 2501 CK The Hague, the Netherlands, and Leiden University Medical Centre, P.O. Box 9600, 2300 RC Leiden, the Netherlands

ARTICLE INFO

Article history:
Received 3 May 2020
Revised 25 April 2021
Accepted 6 June 2021

Keywords:
Stroke care
Centralization
Emergency department

ABSTRACT

When acute stroke care is organised using a “drip-and-ship” model, patients receive immediate treatment at the nearest primary stroke centre followed by transfer to a comprehensive stroke centre (CSC). When stroke care is further centralised into the “direct-to-mothership” model, patients with stroke symptoms are immediately brought to a CSC to further reduce treatment times and enhance stroke outcomes. We investigated the effects of the ongoing centralization in a Dutch urban setting on treatment times of patients with confirmed ischemic stroke in a 4-year period. Next, in a non-randomized controlled trial, we assessed treatment times of patients with suspected ischemic stroke, and treatment times of patients with neurologic disorders other than suspected ischemic stroke, before and after the intervention in the CSC and the decentralized hospitals, the intervention being the change from “drip and ship” into “direct-to-mothership”. Our findings provide support for the ongoing centralization of acute stroke care in urban areas. Treatment times for patients with ischemic stroke decreased significantly, potentially improving functional outcomes. Improvements in treatment times for patients with suspected ischemic stroke were achieved without negative side effects for self-referrals with stroke symptoms and patients with other neurological disorders.

1. Introduction

Stroke is one of the leading causes of mortality and disability worldwide [1]. Over the last decades, the absolute number of people with first stroke has increased and this number is expected to rise in the coming years [2]. In the Netherlands approximately 43.000 people suffer a stroke per year, while this number is approximately 17 million worldwide [3]. Among survivors, there is substantial disability.

Organized acute stroke care by a special multidisciplinary team in the hospital is associated with improved quality of care, a lower mortality and dependency [4–7] and higher patient and caregiver satisfaction [8]. Besides this, the provision of stroke thrombolysis through collaboration results in higher treatment rates [9], and substantial annual cost-savings per patient [10]. Access to stroke care and organisational models within stroke units vary within and between countries [11–13]. In the Netherlands, as in several other

* Corresponding author.
E-mail addresses: c.van.der.linden@haaglandenmc.nl (M.C. VAN DER LINDEN), r.lam@haaglandenmc.nl (R.C. LAM), p.stap@haaglandenmc.nl (P. STAP), c.vandenbrand@dica.nl (C.L. VAN DEN BRAND), t.dofferhoffvermeulen@haaglandenmc.nl (T. VERMEULEN), K.Jellema@haaglandenmc.nl (K. JELLEMA), i.van.den.wijngaard@haaglandenmc.n (I.R. VAN DEN WIJNGAARD).
[1] Both authors contributed equally.

https://doi.org/10.1016/j.healthpol.2021.06.003
0168-8510/

countries, acute stroke services are centralized into “drip and ship” models: patients with a stroke are triaged to the nearest hospital and only transferred to a comprehensive stroke centre (CSC) for endovascular stroke treatment when a large vessel occlusion (LVO) has been demonstrated.

Centralization of stroke care can evolve further into the so-called “direct-to-mothership” model: all patients with suspected stroke are brought immediately to a high capacity, high volume CSC rather than to the nearest hospital. In urban areas with multiple hospitals and short ambulance transport times, this could lead to even faster treatment times, which enhances stroke outcomes [14,15].

In a large part of the The Hague region in the Netherlands further centralization of acute stroke care from a “drip and ship” model into a “direct-to-mothership” model has been realized since January 2016. The number of hospitals offering acute stroke care decreased from three to one, aiming for a higher quality of stroke care, more specifically, a shorter onset-to-groin time for patients with ischemic stroke. While the “direct-to-mothership” model was strongly encouraged by the CSC, it was still allowed to bring patients to the decentralized hospitals. Before implementation, emergency department (ED) staff raised concerns about the impact of the ongoing centralization on the care for patients with neurologic disorders other than stroke, and on the care for self-referrals with symptoms of acute stroke presenting at one of the decentralized hospitals. We hypothesized that patients with neurologic disorders other than stroke would also shift to the CSC due to difficulties in differentiating between acute stroke and less acute neurologic disorders. ED staff had concerns that door-to-physician times and ED patients’ length of stay (LOS) would increase both for self-referrals with stroke symptoms when attending at one of the decentralized hospitals, and for patients with neurologic disorders other than stroke symptoms presenting at the CSC.

The aim of this study was to investigate the effects of the ongoing centralization of acute stroke care from the “drip and ship” model into the “direct-to-mothership” model in the city of The Hague. We assessed the effects on treatment times of patients with confirmed acute ischemic stroke, treatment times of patients with suspected ischemic stroke, and treatment times of patients with neurologic disorders other than suspected acute ischemic stroke.

2. Materials and methods

2.1. Design and setting

2.1.1. Study design

First, we extracted four years of data (2015 to 2018) from the prospective stroke registry. We obtained the number of endovascular stroke treatments (EVTs) and the door-to-groin time (DTGT). DTGT is the door time to the groin puncture at the start of the EVT. Furthermore, we obtained the number of application of intravenous thrombolysis (IVT), including the median door-to-needle time (DTNT) defined as the door time to the start of the IVT. We describe the treatment options of IVT and EVT in Supplement 1. We collected median onset-to-treatment time for all patients with a confirmed ischemic stroke.

Second, a non-randomized controlled trial was used to compare a 7 month pre-intervention period (June 1, 2015 to January 1, 2016) and a 35-month post-intervention period (January 1, 2016 to December 1, 2018), the intervention being the change from “drip and ship” into “direct-to-mothership”. We assessed the treatment times of patients with suspected ischemic stroke, and patients with neurologic disorders other than suspected acute ischemic stroke in two groups: patients presenting for neurology at the CSC and patients presenting for neurology at the decentralized hospitals. We obtained patient level data from the digital hospital registration system of all patients who were assessed by the neurologist. For patients who were transferred between the included hospitals, only the first ED visit was counted. Data on number and type of neurology patients, patient characteristics (age and gender) and visit characteristics (referral status, urgency level, arrival times, door-to-physician time, ED LOS, and disposition (hospital admission yes/no)) are described for the CSC and the decentral hospitals, comparing the pre-intervention period with the post-intervention period. Patients were included in the ‘suspected ischemic stroke’ group when in the patient’s file this diagnosis was listed first in the differential diagnoses after a CT-scan had been performed. We assessed the effect of acute stroke care centralization on treatment times using multivariate analyses, to be able to control for patient characteristics and visit characteristics.

2.1.2. Setting

This study took place in the Hague, the third-largest city in the Netherlands, with a population of over 500,000 and a density of 6.445 per km^2. The neurologists of three collaborating hospitals, including the largest CSC of the region, initiated acute stroke care centralization into the “direct-to-mothership” model at January 1, 2016, appointing one of the three hospitals as CSC and the other two as decentralized centers. The CSC offers hyper-acute stroke care with access to interventional neuro-radiology and neurosurgery 24/7. It is also a level one-trauma center with 55,000 ED visits annually. Both decentralized hospitals have approximately 25,000 ED visits annually. The emergency medical services (EMS) were informed in November and December 2015 about the intervention, and from January 2016 onwards, ambulance nurses were instructed to bring all patients with suspected ischemic stroke directly to the CDC. During the study period, there were no changes in ED management at the hospitals. There was no extra education or change in expertise of the treating EMS staff and ED staff before and after the intervention. At the CSC, attending-level supervision was introduced during peak hours (from noon to 8 pm) during the post-intervention period. Communication to patients and health care professionals about the intervention included announcements in the local newspapers and websites, dissemination of EVT research findings at the professional associations’ websites and presentations by the neurology staff at medical conferences. The clinical pathway of the neurology patients and the healthcare payment system in the Netherlands were unchanged during the study periods.

2.1.3. Analyses

We assessed the numbers of IVT and EVT in absolute numbers and percentages of the total number of confirmed ischemic strokes in the study years 2015 to 2018. We described the median onset-to-treatment time, DTGT, and DTNT with their interquartile ranges (IQR) in the same four years.

We calculated the secondary outcomes in a 42-month study period. Patients’ age, door-to-physician time, and LOS in the decentralized hospitals and the CSC were represented as medians (IQR). We tested differences between the pre-intervention period and the post-intervention period and between self-referrals and non-self-referrals with Mann-Whitney U-tests, due to the non-normal distribution of the metrics. We compared differences in patient and visit characteristics during the pre-intervention period and post-intervention period between the CSC and control hospitals and per patient group using Chi^2 tests.

To investigate the potential moderating influence of type of hospital, disease, and period on door-to-physician time and patients’ ED LOS, we employed a series of analyses of variance (ANOVAs). First, the outcome variables door-to-physician time and patients’ ED LOS were log-transformed. We conducted multivariate regression analyses, including period, hospital, disease, age, gender,

Table 1
Confirmed ischemic stroke, numbers and treatment times.

	2015	2016	2017	2018
Confirmed ischemic stroke episodes N	797	772	881	863
Endovascular stroke treatment N (%)	53 (6.7)	78 (10.1)	107 (12.1)	152 (17.6)
Onset-to-groin time in min, median (IQR)[a]	211 (76)	154 (87)	125 (101)	128 (84)
Door-to-groin time in min, median (IQR)	70 (58)	87 (48)	62 (46)	49 (36)
Intravenous thrombolysis N (%)	163 (20.5)	182 (23.6)	198 (22.3)	207 (24.0)
Onset-to-needle time in min, median (IQR)[a]	79 (53)	71 (31)	76 (55)	75 (52)
Door-to-needle time in min, median (IQR)	31 (39)	27 (21)	24 (18)	22 (19)

[a] Data based on 27 patients (2015), 41 patients (2016), 40 patients (2017), and 53 patients (2018), due to missing values.

referral status, urgency level, arrival times, two-way interactions (all combinations of hospital, disease, period, self-referral and urgency) and three-way interactions (of the same variables) in the models as potential covariates. Using backward stepwise selection, we subsequently removed the largest *p*-values until all *p*-values were smaller than 0.05. Lower order terms with insignificant coefficients were only removed when their higher order terms were removed first.

Interaction plots were created to aid interpretation of the findings. We expressed effect sizes in adjusted odds ratio's (ORs) and their 95% confidence intervals (CI). We used the Statistical Package of the Social Sciences (Windows 26.0, New York, USA) for the analyses. A *p*-value <0.05 was considered statistically significant.

We obtained approval from the research committee of the participating hospitals and from the Ethical Review Board (Southwest Holland).

3. Results

3.1. Patients with confirmed ischemic stroke

During the study years 2015 to 2018, the number of patients with confirmed ischemic stroke remained similar with approximately 800 per year in the CSC and the decentralized hospitals together. The number of patients undergoing EVT increased from 53 (6.7%) in 2015 to 152 (17.6%) in 2018 while their onset-to-groin time decreased from a median of 211 minutes (IQR 76) in 2015 to 128 minutes (IQR 84) in 2018. DTGT decreased from 70 minutes, IQR 58 (in 2015) to 49 minutes, IQR 36 (in 2018). The number of patients undergoing IVT increased from 163 (20.5%) in 2015 to 207 (24.0%) in 2018, while the onset-to-needle time did not change significantly. The median DTNT decreased from 31 minutes (IQR 39) in 2015 to 22 minutes (IQR 19) in 2018 (Table 1, Supplements 2 and 3).

3.2. Neurology patient and visit characteristics

During the 42-month study period, 21,581 visits for neurology were registered at the EDs, 3313 (473 per month) in the 7-month pre-intervention period and 18268 (522 per month) in the 35-month post-intervention period (see Flow chart, Supplement 4). During the pre-intervention period, 76.1% of these visits were registered at the CSC (n=2521) and 23.9% (n=792) were registered at the decentralized locations. This ratio was similar during the post-intervention period, in which 76.7% (n=14012) were registered at the CSC and 23.3% (n=4256) at the decentralized locations (p=0.45).

In the decentralized hospitals, the number of ED visits for suspected ischemic stroke decreased from 10.6 to 5.6 per month, and the number of ED visits for other neurologic disorders increased from 102.6 to 116.0 visits per month. At the CSC, the number of visits increased, both for suspected ischemic stroke (from 60.3 to 70.5 per month) and for other neurologic disorders (from 299.9 to 329.9 visits per month), although no statistically significant difference was reached.

The monthly numbers of patients presenting with suspected ischemic stroke and patients with other neurologic disorders showed no trend break in the graphs at the time the intervention took place (month 8) (Supplement 5 and 6).

At the decentralized hospitals, there were no differences between the two periods in number of self-referrals, gender, urgency level and time of arrival (Table 2). Patients in the post-intervention period were younger (median 58 y vs. 62 y in the pre-intervention period, p=0.01), and were less often admitted to the hospital (30.6% vs. 44.2% in the pre-intervention period ($p<0.001$). At the CSC, patients in the post-intervention period were less often self-referred ($p<0.001$), and they were older ($p<0.001$). They presented more often with urgent disorders (p=0.001), but were less likely to be admitted to the hospital ($p<0.001$).

Analyses of the decentralized hospitals separately showed that the number of patient visits for suspected ischemic stroke decreased, and the number of patient visits for other neurologic disorders increased in both decentral hospitals. There were no differences between pre- and post-intervention period in number of self-referrals, urgency levels, and time of arrival in the hospitals, but patients in one of the decentral hospitals were younger (p=0.001) and less often admitted to the hospital (p<0.001) during the post-intervention period (Data not shown).

3.3. Neurology patients' treatment times and total length of stay at the emergency department

At the decentralized hospitals, median door-to-physician times for patients with suspected stroke were slightly longer in the post-intervention period, while these were shorter for patients with neurologic disorders other than stroke. At the CSC, door-to-physician times and ED LOS in the post-intervention period were significantly shorter for all patient groups compared with the pre-intervention period. For self-referrals presenting with stroke symptoms, median ED LOS decreased significantly regardless of hospital type (Table 3).

3.4. The effect of centralization on door-to-physician time and total length of stay

The multivariate regression analysis including period, hospital, disease, age, gender, referral status, urgency level, arrival times, two-way interactions (all combinations of hospital, disease, period, self-referral and urgency) and three-way interactions (same variables) shows the effect of these variables on door-to-physician time and LOS (Table 4). Corrected for the other variables, arriving in the post-intervention period, having a higher age, being male and arriving during the evening or night shift significantly decreased door-to-physician times. Significant interactions exist between disease, self-referral, hospital type and urgency. For example, patients with stroke have significant shorter door-to-physician times than patients with other neurologic disorders, especially for

Table 2
Patient and visit characteristics (N=21581).

	Pre-Intervention 7 months	Post-Intervention 35 months	Odds Ratio (95% CI)	P[a]
DECENTRALIZED HOSPITALS (N=5048)				
Neurology visits n (per month)	792 (113.1)	4256 (121.6)		
Suspected ischemic stroke n (per month)	74 (10.6)	196 (5.6)	0.47 (0.35, 0.62)	<0.001
Other neurology disorders n (per month)	718 (102.6)	4060 (116.0)		
Self-referred n (%)	281 (35.5)	1518 (35.7)	1.01 (0.86, 1.18)	0.92
Median age in years (IQR)	62 (41-79)	58 (42-79)		0.01
Sex, female	440 (55.6)	2314 (54.4)	0.95 (0.82, 1.11)	0.54
Urgency level, urgent n (%)[b]	633 (80.0)	3380 (79.4)	0.96 (0.80, 1.17)	0.71
Time of arrival n (%)				0.33
Day shift	483 (61.0)	2476 (58.2)		
Evening shift	250 (31.6)	1452 (34.1)		
Night shift	59 (7.4)	328 (7.7)		
Hospital admission n (%)[c]	341 (44.2)	1284 (30.6)	0.56 (0.48, 0.65)	<0.001
CSC (n=16533)				
Neurology visits n (per month)	2521 (360.1)	14012 (400.3)		
Suspected acute stroke n (per month)	422 (60.3)	2467 (70.5)	1.06 (0.95, 1.19)	0.29
Other neurology disorders n (per month)	2099 (299.9)	11545 (329.9)		
Self-referred n (%)	514 (20.4)	2400 (17.1)	0.81 (0.73, 0.90)	<0.001
Median age in years (IQR)	57 (39-72)	59 (40-74)		<0.001
Sex, female n (%)	1229 (48.8)	7075 (50.5)	1.07 (0.99, 1.17)	0.11
Urgency level, urgent n (%)[b]	2103 (83.5)	12062 (86.1)	1.23 (1.09, 1.38)	0.001
Time of arrival n (%)				0.56
Day shift	1250 (49.6)	6871 (49.0)		
Evening shift	969 (38.4)	5532 (39.5)		
Night shift	302 (12.0)	1609 (11.5)		
Hospital admission n (%)[c]	1259 (50.0)	6428 (45.9)	0.85 (0.78, 0.92)	<0.001

[a] Significances were calculated using Chi^2-tests (number of visits, referral status, sex, urgency level, time of arrival, and hospital admission) and the Mann-Whitney U test (age).
[b] Urgency level: 2 missing values in the decentral hospitals: 1 in the pre-intervention period and 1 in the post-intervention period, 6 missing values in the CSC, 2 in the pre-intervention period and 4 in the post-intervention period.
[c] Hospital admission: 80 missing values in the decentral hospitals: 21 in the pre-intervention period and 59 in the post-intervention period, and 6 missing values in the CSC in the pre-intervention period.

Table 3
Treatment times and total ED LOS

	Pre-intervention	Post-intervention	P[a]
DECENTRALIZED HOSPITALS (n=5048)			
Patients with suspected ischemic stroke n (per month)	74 (10.6)	196 (5.6)	
Median door-to-physician time in min (IQR)[b]	3.00 (1.00-5.00)	4.00 (2.00-8.00)	0.02
Median LOS in min (IQR)[b]	189.00 (145.00-262.50)	210.00 (133.00-290.00)	0.77
Self-referrals with suspected acute stroke n (per month)	25 (3.6)	59 (1.7)	
Median door-to-physician time (IQR)[c]	3.00 (2.00-5.00)	3.00 (2.00-7.00)	0.42
Median LOS in min (IQR)[c]	186.50 (127.75-254.25)	138.50 (53.25-236.00)	0.03
Patients with neurologic disorders other than stroke n (per month)	718 (102.6)	4060 (116.0)	
Median door-to-physician time in min (IQR)[d]	4.00 (2.00-10.00)	4.00 (2.00-8.00)	0.03
Median LOS in min (IQR)[d]	154.00 (105.00-214.00)	151.00 (105.00-209.00)	0.27
CSC (N=16533)			
Patients with suspected ischemic stroke n (per month)	422 (60.3)	2467 (70.5)	
Median door-to-physician time in min (IQR)[b]	2.00 (0.00-6.75)	2.00 (0.00-5.00)	0.004
Median LOS in min (IQR)[b]	203.50 (149.00-278.00)	185.00 (130.00-257.00)	<0.001
Self-referrals with suspected acute stroke n (per month)	35 (5.0)	205 (5.9)	
Median door-to-physician time in min (IQR)[c]	6.00 (3.00-14.00)	4.00 (1.75-9.25)	0.03
Median LOS in min (IQR)[c]	248.00 (178.00-307.00)	202.50 (133.75-285.25)	0.04
Patients with neurologic disorders other than stroke n (per month)	2099 (299.9)	11545 (329.9)	<0.001
Median door-to-physician time in min (IQR)[d]	4.00 (2.00-10.00)	3.00 (1.00-8.00)	<0.001
Median LOS in min (IQR)[d]	204.00 (144.00-281.00)	186.00 (131.00-257.00)	

[a] Significances were calculated using the Mann-Whitney test.
[b] Missing values in the decentral hospitals: 1 in the pre-intervention period and 1 in the post-intervention period and in the CSC 2 in the pre-intervention period and 41 in the post-intervention period.
[c] Missing values in the decentral hospitals: 1 in the pre-intervention period and 1 in the post-intervention period, and in the CSC 3 in the intervention period.
[d] Missing values in the decentral hospitals: 11 in the pre-intervention period and 13 in the post-intervention period, and in the CSC 3 in the pre-intervention period and 32 in the post-intervention period.

Table 4
The impact of centralization on door-to-physician time and total length of stay, adjusting for other potential confounders.

	Exp (B)	95% CI	*P*
Variables associated with log-transformed door-to-physician time			
Period (pre-intervention and post-intervention period)	-0.064	-0.103, -0.025	0.001
Disease (stroke and other neurological disorders)	-0.061	-0.110, -0.011	0.016
Type of hospital (CSC and decentralized hospitals)	0.271	0.194, 0.347	<0.001
Age, log-transformed	-0.072	-0.093, -0.052	<0.001
Arrival during evening shift	-0.057	-0.088, -0.026	<0.001
Arrival during night shift	-0.419	-0.469, -0.369	<0.001
Gender, male	-0.036	-0.065, -0.007	0.016
Self-referral	0.445	0.366, 0.523	<0.001
Self-referral * Disease, two-way interaction	-0.205	-0.333, -0.052	<0.001
Self-referral * Urgency, two-way interaction	-0.174	-0.276, -0.073	0.001
Self-referral * Urgency * Hospital, three-way interaction	0.306	0.225, 0.386	<0.001
Urgency, urgent triage level	0.082	0.001, 0.164	0.048
Urgency * Hospital, two-way interaction	-0.268	-0.357, -0.180	<0.001
	Exp (B)	95% CI	*P*
Variables associated with patients' log-transformed length of stay			
Period (pre-intervention and post-intervention period)	0.101	0.011, 0.191	0.029
Disease (stroke and other neurological disorders)	0.299	0.162, 0.437	<0.001
Type of hospital (CSC and decentralized hospitals)	1.358	1.228, 1.488	<0.001
Hospital * Disease, two-way interaction	-0.194	-0.266, -0.123	<0.001
Period * Hospital, two-way interaction	-0.099	-0.147, -0.050	<0.001
Age, log-transformed	0.154	0.143, 0.165	<0.001
Arrival during evening shift	-0.051	-0.067, -0.035	<0.001
Arrival during night shift	-0.195	-0.220, -0.170	<0.001
Urgent triage level	0.874	0.825, 0.922	<0.001
Urgency * Hospital, two-way interaction	-0.847	-0.903, -0.791	<0.001
Self-referral	0.620	0.540, 0.699	<0.001
Self-referral * Hospital, two-way interaction	-0.605	-0.692, -0.518	<0.001
Self-referral * Period, two-way interaction	-0.062	-0.111, -0.013	0.013
Self-referral * Urgency, two-way interaction	-0.720	-0.796, -0.643	<0.001
Self-referral * Urgency * Hospital, three-way interaction	0.780	0.683, 0.877	<0.001

Multivariate regression models adjusted for period, hospital, disease, age, gender, referral status, urgency level, arrival times, two-way interactions (hospital * disease, period * hospital, period * disease, self-referral * hospital, self-referral * period, self-referral * disease, self-referral * urgency, urgency * period, and urgency * hospital) and the three-way interaction (type of hospital * disease * period, self-referral * urgency * hospital and self-referral * urgency * period). Using backward stepwise selection, the largest *p*-values were sequentially removed until all *p*-values were smaller than 0.05.

non-self-referrals. Urgent patients at the CSC have shorter door-to-physician times than urgent patients at the decentralized hospital. In the decentralized hospitals, door-to-physician time is similar for urgent and non-urgent patients.

Corrected for other variables, having a stroke and being of higher age increases patients' ED LOS. Arriving during the evening or night shift decreases patients' ED LOS. Significant interactions exist between disease, period, being a self-referral, hospital type and urgency. For example, the intervention had a larger impact on patients' ED LOS at the CSC, although in both hospital types LOS was shorter in the post intervention period. Also, non-urgent self-referrals had shorter ED LOS than urgent self-referrals, regardless in which hospital they presented (Table 4, Supplements 7 and 8).

4. Discussion

The effects of stroke care units and centralized care on the health outcomes of stroke patients are extensively explored in several countries and different health care systems [5,7,8,16–24]. Comprehensive stroke centres are associated with improved functional outcomes and a more frequent use of reperfusion therapy [25]. To our knowledge, this is the first study to evaluate the ongoing centralization from "drip and ship" into "direct-to-mothership" on stroke patients' treatment times as well as on treatment times of self-referrals with suspected stroke, and on patients with neurologic disorders other than stroke in a CSC and in decentralized centers.

5. Principal findings

After centralizing acute stroke care from "drip and ship" into "direct-to-mothership", the number of patients with suspected acute ischemic stroke decreased in the decentralized hospitals, while increasing in the CSC. Probably, before the intervention, some of the patients with suspected ischemic stroke would have been brought to one of the decentralized hospitals before being transported to the CSC. Consistent with the international trend, we observed an increase in patients who underwent IVT and EVT, while the total number of patients with confirmed ischemic stroke remained similar. The onset-to-groin time decreased from a median of 211 minutes to 128 minutes, an important finding since preventing delay in time between stroke and recanalization for acute ischemic stroke is associated with better functional outcomes [26].

Monthly measurements of the number of patients showed no deviation from the trend at the time the intervention (change from "drip and ship" model into "direct-to-mothership" model) took place. A more gradual decrease in number of patients with suspected ischemic stroke occurred in the decentral hospitals. Simultaneously, the number of patient visits for other neurologic disorders increased, mostly due to an increase in patients with mild traumatic brain injuries. The latter can be explained by the ageing population and hence more falls [27].

Overall, patients less often needed hospital admission during the post-intervention period. While this could suggest a less sick population, the higher urgency levels and higher median age during the post-intervention period suggests differently. It is possible that attending-level supervision, which was common practice in the post-intervention period but not in the pre-intervention period, led to a decrease in hospital admissions. In a previous study, we showed a 10% decrease in total number of clinical admissions for neurology after the introduction of a dedicated neurologist present at the ED during peak hours [28].

After the intervention, LOS of patients with neurologic disorders other than suspected ischemic stroke presenting at the CSC decreased significantly as well. Again, the presence of a dedicated neurologist at the ED may have contributed to this finding. In previous research, median LOS decreased with 30 minutes per patient after the introduction of a dedicated neurologist at the ED [28]. Patients with neurologic disorders other than ischemic stroke also may benefit from the enhanced focus on treatment times of patients with ischemic stroke. This is an important finding, since the treatment for various acute neurologic disorders other than ischemic stroke also improves with rapid intervention, for example in patients with intra parenchymal hemorrhage, subarachnoid hemorrhage, increased intracranial pressure or meningitis.

While it was hypothesized that ED patients' LOS and door-to-physician times would increase both for self-referrals with suspected ischemic stroke when attending at one of the decentralized hospitals, and for patients with neurologic disorders other than suspected ischemic stroke presenting at the CSC, our findings show otherwise. Self-referrals presenting with stroke symptoms experienced no change in door-to-physician times at the decentral hospital, but their ED LOS was significantly shorter than in the pre-intervention period. At the CSC, both the door-to-physician times as well as total ED LOS decreased for self-referrals with stroke symptoms. For patients with other neurological disorders, door-to-physician times were shorter in the post-intervention period at both the decentralized hospital and the CSC, and ED LOS decreased with a significant 18 min per patient at the CSC. This may indicate better logistic processes during the post-intervention period. An enhanced focus on an efficient stroke process may improve other processes of care for related patient groups at the same time. Improved awareness in professionals as well as among the public may also play its part.

The clinical consequence of our results is that centralization of stroke care in a highly urbanized setting, especially with regard to stroke interventions, leads to improved care for patients with stroke. Efforts should be made to improve cooperation of stroke care centres and centralization should be considered.

Stroke systems of care continue to evolve rapidly and resources need to be allocated to allow for this, given the unprecedented but time-sensitive benefit of EVT on clinical outcomes. The delays in the drip and ship model have led to a pragmatic recommendation by the American Stroke Association/American Heart Association Mission Lifeline algorithm to consider direct transport to CSCs, bypassing a decentralized hospital, if the additional travel time is <15 minutes [29]. However, in many countries the drip and ship model is still used and advocated with the argument that the mothership model delays initial treatment times for IVT and could potentially lead to overcrowding in CSCs. Our study shows otherwise and supports the direct transport to CSC in a metropolitan area with short driving times (i.e. less than 15minutes additional travel time) [30]. In the thrombectomy era of stroke care, we should tailor our health systems and interfacility collaborations to best meet the local and regional needs of our patients [31]. Ongoing research will likely provide the much needed answers whether our increasing ability to identify patients with stroke due to LVO in the prehospital setting will lead to better treatment times and patient outcomes [32].

6. Strengths and weaknesses

We had a large sample and captured detailed data on patient visits to three EDs in one city. Therefore, this study was able to provide unique insights into a broad range of (potential) effects of centralization of stroke care. Additionally, the use of a pre-post design supplemented with monthly measurements, enabled us to assess changes in neurologic patient flow meticulously. A downside of before-and-after analysis is that it is impossible to control for secular trends and other covariates. However, by including patient and visit characteristics as well as the interaction terms into regression models, we provided valuable insights into the effects of ongoing centralization on patients' treatment times. Some of our findings call for more research, such as the impact of gender on door-to-physician time.

Additionally, there were several limitations. Our study took place in an urban setting in the Netherlands, which limits our findings to metropolitan areas in higher income countries with similar healthcare provisions. The current research project does not focus on patients with longer (i.e. > 15 min. additional) transportation times. Second, we lacked data on patient outcomes such as dependence or disability (for the patients with an acute ischemic stroke), and patient satisfaction and missed diagnoses (for the patients with neurological disorders other than stroke). We mainly focused on treatment times, measured from onset to start of the treatment, from ED arrival to start of treatment, and total ED LOS. Previous studies convincingly showed that decreased onset-to-groin times and decreased door-to-needle times for stroke patients are strongly associated with improved functional outcome [33,34].

Third, in our study, patients were included in the 'suspected ischemic stroke' group when in the patient's file this diagnosis was listed first in the differential diagnoses after a CT-scan had been performed. We did not identify patients with intracerebral haemorrhage as stroke patients, therefore, these patients are included in the 'Other neurology disorders' group. Since organised stroke care is beneficial to patients with intracerebral haemorrhage as well as ischemic stroke [35], this classification might explain part of the positive effects seen in the 'Other neurology disorders' group.

Fourth, we did not study cost-effectiveness in the current study. Multiple studies show that the centralization of acute stroke care is a cost-effective and even cost-saving measure to improve stroke outcomes [36,37]. Our findings suggest that including possible side effects of centralization will not change these positive conclusions: for patients with neurologic disorders other than an ischemic stroke door-to-physician times decreased at the decentral hospitals as well as the CSC. Significantly shorter ED LOSs were observed at the CSC. The latter may be a positive side effect of centralization.

7. Conclusions

Our findings provide support for the ongoing centralization of acute stroke care in urban settings with short driving distances (<15 minutes time) showing significantly shorter treatment times for patients with ischemic stroke as well as for self-referring patients with stroke symptoms and patients with neurologic disorders other than suspected acute ischemic stroke.

Funding

This study was funded by a grant from The Netherlands Organisation for Health Research and Development (ZonMw) in collaboration with the National Health Care Institute, grant no. 516022515. The funding source had no involvement in the study design, the collection, analysis and interpretation of the data, nor in the writ-

ing of the report and in the decision to submit the article for publication.

Ethics approval and consent to participate

The ethical review committee of Southwest Holland granted approval and exemption. Patient consent was not required.

Declaration of Competing Interest

All authors work in the study setting, except for Naomi van der Linden, who currently works at the University of Twente but was employed by AstraZeneca Netherlands, a pharmaceutical company, during this study. Crispijn van den Brand worked in the study setting and is currently employed by the Dutch Institute for Clinical Auditing.The authors declare that they have no competing interests

CRediT authorship contribution statement

M. Christien VAN DER LINDEN: Conceptualization, Data curation, Formal analysis, Writing – original draft. **Naomi VAN DER LINDEN:** Formal analysis, Writing – original draft. **Rianne C. LAM:** Investigation. **Peter STAP:** Investigation. **Crispijn L. VAN DEN BRAND:** Writing – review & editing. **Tamara VERMEULEN:** resources. **Korné JELLEMA:** Writing – review & editing. **Ido R. VAN DEN WIJNGAARD:** Conceptualization, Writing – review & editing, Supervision.

Acknowledgement

The authors thank Willeke Floor-de Winter, Thomas Vissers, Annemarie van der Velden, and Alex Waber for their invaluable help.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.healthpol.2021.06.003.

References

[1] Poos, M.J.J.C., Gommer, A.M., Rodriguez, M. Sterfte beroerte naar type 2019 [In Dutch] 2020 [updated 04-09-2020]. Available from: https://www.volksgezondheidenzorg.info/onderwerp/beroerte/cijfers-context/sterfte#node-sterfte-beroerte-naar-type.
[2] Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet 2014;383(9913):245–55.
[3] Bots, M.L., Buddeke, J., Van Dis, I., Vaartjes, I., Visseren, F.L.J.. Hart- en vaatziekten in Nederland, 2016. Den Haag, 2016. Available from: https://www.hartstichting.nl/getmedia/06fb9c92-a1f7-4135-a635-ff73680bfaa6/cijferboek-hartstichting-hart-vaatziekten-nederland-2016.pdf.
[4] Langhorne P, Lewsey JD, Jhund PS, Gillies M, Chalmers JW, Redpath A, et al. Estimating the impact of stroke unit care in a whole population: an epidemiological study using routine data. J Neurol Neurosurg Psychiatry 2010;81(12):1301–5.
[5] Morris S, Hunter RM, Ramsay AI, Boaden R, McKevitt C, Perry C, et al. Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. BMJ 2014;349:g4757.
[6] Tung Y-C, Chang G-M. The relationships among regionalization, processes, and outcomes for stroke care: a nationwide population-based study. Medicine 2016;95(15).
[7] Ramsay AI, Morris S, Hoffman A, Hunter RM, Boaden R, McKevitt C, et al. Effects of centralizing acute stroke services on stroke care provision in two large metropolitan areas in England. Stroke 2015;46(8):2244–51.
[8] Moynihan B, Paul S, Markus HS. User experience of a centralized hyperacute stroke service: a prospective evaluation. Stroke 2013;44(10):2743–7.
[9] Price CI, Clement F, Gray J, Donaldson C, Ford GA. Systematic review of stroke thrombolysis service configuration. Expert Rev Neurother 2009;9(2):211–33.
[10] Lahr MM, van der Zee DJ, Luijckx GJ, Vroomen PC, Buskens E. Centralising and optimising decentralised stroke care systems: a simulation study on short--term costs and effects. BMC Med Res Methodol 2017;17(1):5.
[11] Aguiar de Sousa D, von Martial R, Abilleira S, Gattringer T, Kobayashi A, Gallofré M, et al. Access to and delivery of acute ischaemic stroke treatments: a survey of national scientific societies and stroke experts in 44 European countries. European stroke journal 2019;4(1):13–28.
[12] Wiedmann S, Hillmann S, Abilleira S, Dennis M, Hermanek P, Niewada M, et al. Variations in acute hospital stroke care and factors influencing adherence to quality indicators in 6 European audits. Stroke 2015;46(2):579–81.
[13] van Veenendaal P, Yan B, Churilov L, Dowling R, Bush S, Mitchell P. Endovascular clot retrieval by hub-and-spoke service delivery is feasible compared with direct-to-mothership. Cerebrovasc Dis 2018;46(3-4):170–5.
[14] Ismail M, Armoiry X, Tau N, Zhu F, Sadeh-Gonik U, Piotin M, et al. Mothership versus drip and ship for thrombectomy in patients who had an acute stroke: a systematic review and meta-analysis. J Neurointerv Surg 2019;11(1):14–19.
[15] Venema E, Groot AE, Lingsma HF, Hinsenveld W, Treurniet KM, Chalos V, et al. Effect of interhospital transfer on endovascular treatment for acute ischemic stroke. Stroke 2019;50(4):923–30.
[16] Campbell JT, Bray BD, Hoffman AM, Kavanagh SJ, Rudd AG, Tyrrell PJ. The effect of out of hours presentation with acute stroke on processes of care and outcomes: analysis of data from the Stroke Improvement National Audit Programme (SINAP). PLoS ONE 2014;9(2):e87946.
[17] Douw K, Nielsen CP, Pedersen CR. Centralising acute stroke care and moving care to the community in a Danish health region: challenges in implementing a stroke care reform. Health Policy 2015;119(8):1005–10.
[18] Fuentes B, Diez-Tejedor E. Stroke units: many questions, some answers. Int J Stroke 2009;4(1):28–37.
[19] Fulop N, Boaden R, Hunter R, McKevitt C, Morris S, Pursani N, et al. Innovations in major system reconfiguration in England: a study of the effectiveness, acceptability and processes of implementation of two models of stroke care. Implement Sci 2013;8:5.
[20] Kwan J. Care pathways for acute stroke care and stroke rehabilitation: from theory to evidence. J Clin Neurosci 2007;14(3):189–200.
[21] Kwan J, Sandercock P. In-hospital care pathways for stroke. Cochrane Database Syst Rev 2004(4):CD002924.
[22] Masjuan J, Alvarez-Sabin J, Arias-Rivas S, Blanco M, de Felipe A, Escudero–Martinez I, et al. Urgent stroke care in hospitals with a stroke unit. Quick project. Rev Neurol 2016;62(7):303–10.
[23] Rudd AG, Hoffman A, Grant R, Campbell JT, Lowe D. Stroke thrombolysis in England, Wales and Northern Ireland: how much do we do and how much do we need? J Neurol Neurosurg Psychiatry 2011;82(1):14–19.
[24] Turner S, Ramsay A, Perry C, Boaden R, McKevitt C, Morris S, et al. Lessons for major system change: centralization of stroke services in two metropolitan areas of England. J Health Serv Res Policy 2016;21(3):156–65.
[25] Xian Y, Holloway RG, Chan PS, Noyes K, Shah MN, Ting HH, et al. Association between stroke center hospitalization for acute ischemic stroke and mortality. JAMA 2011;305(4):373–80.
[26] He AH, Churilov L, Mitchell PJ, Dowling RJ, Yan B. Every 15-min delay in recanalization by intra-arterial therapy in acute ischemic stroke increases risk of poor outcome. Int J Stroke 2015;10(7):1062–7.
[27] Van den Brand CL, Karger LB, Nijman S, Hunink MG, Patka P, Jellema K. Traumatic brain injury in the Netherlands, trends in emergency department visits, hospitalization and mortality between 1998 and 2012. Eur J Emerg Med 2018;25(5):355–61.
[28] van der Linden MC, van den Brand CL, van den Wijngaard IR, de Beaufort RAY, van der Linden N, Jellema K. A dedicated neurologist at the emergency department during out-of-office hours decreases patients' length of stay and admission percentages. J Neurol 2018;265(3):535–41.
[29] The American Heart Association and American Stroke Association (AHA/ASA), Mission: Lifeline Stroke. Severity-based stroke triage algorithm for EMS 2018. Available from: https://www.heart.org/en/professional/quality-improvement/mission-lifeline/mission-lifeline-stroke.
[30] Zachrison KS, Khatri P. Self-driven prehospital triage decisions for suspected stroke—another step closer. JAMA Neurol 2021;78(2):146–8.
[31] Southerland AM, Park MS, Switzer JA. Thinking outside the mothership: taking the interventional stroke team on the road. Stroke 2020;51(12):3476–8.
[32] Abilleira S, Pérez de la Ossa N, Jiménez X, Cardona P, Cocho D, Purroy F, et al. Transfer to the local stroke center versus direct transfer to endovascular center of acute stroke patients with suspected large vessel occlusion in the Catalan territory (RACECAT): Study protocol of a cluster randomized within a cohort trial. Int J Stroke 2019;14(7):734–44.
[33] Mulder M, Jansen I, Goldhoorn R, Venema E, Chalos V, Compagne K, et al. Time to endovascular treatment and outcome in acute ischemic stroke: MR CLEAN Registry results. Circulation 2018;138(3):232–40.
[34] Saver JL, Goyal M, Van der Lugt A, Menon BK, Majoie CB, Dippel DW, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. JAMA 2016;316(12):1279–89.
[35] Langhorne P, Fearon P, Ronning OM, Kaste M, Palomaki H, Vemmos K, et al. Stroke unit care benefits patients with intracerebral hemorrhage: systematic review and meta-analysis. Stroke 2013;44(11):3044–9.
[36] Freriks R, Mierau J, Buskens E, Pizzo E, Luijckx G, van der Zee D, et al. Centralising acute stroke care within clinical practice in the Netherlands: lower bounds of the causal impact. BMC Health Serv Res 2020;20(1):103.
[37] Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, et al. Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: a comparative effectiveness before and after model. PLoS ONE 2013;8(8):e70420.