Effects of Centralizing Acute Stroke Services on Stroke Care Provision in Two Large Metropolitan Areas in England

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Background and Purpose—In 2010, Greater Manchester and London centralized acute stroke care into hyperacute units (Greater Manchester=3, London=8), with additional units providing ongoing specialist stroke care nearer patients’ homes. Greater Manchester patients presenting within 4 hours of symptom onset were eligible for hyperacute unit admission; all London patients were eligible. Research indicates that postcentralization, only London’s stroke mortality fell significantly more than elsewhere in England. This article attempts to explain this difference by analyzing how centralization affects provision of evidence-based clinical interventions.

Methods—Controlled before and after analysis was conducted, using national audit data covering Greater Manchester, London, and a noncentralized urban comparator (38623 adult stroke patients, April 2008 to December 2012). Likelihood of receiving all interventions measured reliably in pre- and postcentralization audits (brain scan; stroke unit admission; receiving antplatelet; physiotherapist, nutrition, and swallow assessments) was calculated, adjusting for age, sex, stroke type, consciousness, and whether stroke occurred in-hospital.

Results—Postcentralization, likelihood of receiving interventions increased in all areas. London patients were overall significantly more likely to receive interventions, for example, brain scan within 3 hours: Greater Manchester=65.2% (95% confidence interval=64.3–66.2); London=72.1% (71.4–72.8); comparator=55.5% (54.8–56.3). Hyperacute units were significantly more likely to provide interventions, but fewer Greater Manchester patients were admitted to these (Greater Manchester=39%; London=93%). Differences resulted from contrasting hyperacute unit referral criteria and how reliably they were followed.

Conclusions—Centralized systems admitting all stroke patients to hyperacute units, as in London, are significantly more likely to provide evidence-based clinical interventions. This may help explain previous research showing better outcomes associated with fully centralized models. (Stroke. 2015;46:2244-2251. DOI: 10.1161/STROKEAHA.115.009723.)

Key Words: centralization ■ evaluation ■ quality indicators ■ regional variation ■ stroke care ■ stroke units ■ systems of care

Stroke care based on evidence of clinical effectiveness (eg, access to stroke specialists, rapid scanning, assessment, treatments, and therapies, referred to here as evidence-based clinical interventions) is associated with better patient outcomes.1-5 Benefits include reductions in mortality, length of stay, and disability and increases in independence and quality of life.

Some health systems have centralized their stroke services to create a smaller number of high volume specialist
different models of centralization are associated with different outcomes. However, the mechanisms underlying this effect are unclear. This article attempts to explain the differences in clinical outcomes by analyzing the impact of 2 different models of centralization on provision of evidence-based clinical interventions.

In 2010, stroke services in Greater Manchester (population 2.68 million people) and London (population 8.17 million people) were centralized, with the intention of addressing significant variations in care, whereby many stroke patients did not receive evidence-based clinical interventions. There was little evidence about how best to ensure stroke patients receive the full range of interventions, and though centralization had been proposed for large metropolitan areas, there was little evidence about how best to centralize stroke services. Consequently, Greater Manchester and London selected significantly different models of centralization, reflecting local priorities and stakeholder preferences, for example, in relation to equitable and timely access to services, patient safety, and resource use.

Precentralization, suspected stroke patients were taken to the nearest hospital admitting acute stroke patients: there were 12 such hospitals in Greater Manchester and 30 in London, providing a variety of acute and rehabilitation stroke services (see Figure 1). In each area, stroke services were centralized into a small number of hyperacute stroke units providing care over the first 72 hours after stroke, including assessment by specialized stroke medical teams, brain imaging, and thrombolysis, if appropriate; a larger number of units provided ongoing specialist stroke care nearer to patients’ homes. A major difference between the 2 areas concerned eligibility criteria for hyperacute unit admission. In Greater Manchester, patients presenting within 4 hours of developing symptoms were eligible for admission to 1 of 3 hyperacute units: a Comprehensive Stroke Center, admitting patients at any time, and 1 Primary Stroke Centres (PSCs), admitting patients 7 AM to 7 PM, Monday to Friday (Figure 1A). Patients presenting outside 4 hours were admitted to their nearest District Stroke Center (DSC), which provided all aspects of acute stroke care required beyond the first 4 hours; out of hours, PSCs operated a DSC service. In London, all stroke patients were eligible for treatment in 1 of 8 Hyperacute Stroke Units (HASUs), which admitted stroke patients at any time, and provided the first 72 hours of care; patients were then transferred to the community or to 1 of 24 Stroke Units (SUs), which provided acute rehabilitation services until patients were ready to return to the community (Figure 1B). The contrasting models represent an opportunity to analyze different centralization models.

Recent research indicates that although both Greater Manchester and London centralizations were associated with significantly greater reductions in length of stay, only the London centralization was associated with a significantly greater reduction in stroke patient mortality than in the rest of England. In this article, we examine whether this important difference in outcomes can be explained by (1) the impact of centralizations on provision of evidence-based clinical interventions and (2) differences between the Greater Manchester and London models’ eligibility criteria for admission to hyperacute unit and how reliably these criteria were followed.

**Methods**

**Design**

This study used a controlled before and after design. It analyzed risk-adjusted likelihood of stroke patients receiving evidence-based clinical interventions in Greater Manchester and London, pre- and postcentralization, compared with urban areas of England where acute stroke services had not been centralized (hereafter referred to as the ‘comparator’).

**Data**

Patient-level data were drawn from 2 national audits organized by the Royal College of Physicians: precentralization, the National Sentinel Stroke Clinical Audit, conducted from April to August 2008, was used; postcentralization, the Stroke Improvement National Audit Program (SINAP), which ran from April 2010 to December 2012 was used. Reflecting the implementation dates for the centralizations, the Greater Manchester postcentralization period was April 2010 to December 2012 inclusive, whereas London’s was July 2010 to December 2012 inclusive. Data collected in the 2 audits differed: Sentinel 2008 collected a snapshot of ≤60 patients per participating stroke service, whereas SINAP collected data for all patients receiving stroke care. Consequently, postcentralization data cover significantly more patients.

The analysis included data submitted by all hospitals providing acute stroke care in Greater Manchester, London, and a comparator area formed of hospitals providing acute stroke care in 2 parts of England (North West England, excluding Greater Manchester, and North East England), where local documents showed no equivalent

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**Figure 1.** Simplified summary of stroke service models pre- and postcentralization. A, Both areas, precentralization. B, Greater Manchester, postcentralization. C, London, postcentralization. CSC indicates Comprehensive Stroke Center, Greater Manchester; DSC, District Stroke Center, Greater Manchester; HASU, Hyperacute Stroke Unit, London; PSC, Primary Stroke Center, Greater Manchester; Stroke unit/ward, precentralization stroke unit, combining acute and rehabilitation functions; and SU, Stroke Unit, London.
centralization had occurred. The comparator was limited to hospitals in urban settings equivalent to Greater Manchester and London (classified as major urban by the UK Office for National Statistics); it covered 1.8 million people, and its level of participation in national audits was equivalent to Greater Manchester and London (details available in the online-only Data Supplement). Although Sentinel 2008 had uniformly high participation across England, participation in SINAP was variable in several areas of England, with many hospitals submitting little or no data. These differing participation levels meant the rest of England could not act as the comparator. Consequently, data for 56,100 stroke patients (7300 before, 48,700 after) were excluded. Data for all patients diagnosed with stroke (intracerebral hemorrhage or cerebral infarction) were included, both those occurring in-hospital and outside hospital. Patients with invalid data were excluded.

Measures
We analyzed all evidence-based clinical interventions that had been measured consistently in both audits. These measures were calculated from arrival at hospital (or symptom-onset if occurring in-hospital) and assessed whether patients had their first brain scan within 3 and 24 hours of arrival (cut-off points identified in the baseline audit national report reflecting time to scan to support administration of thrombolysis, and national guidance to scan within 24 hours); were admitted to a stroke unit within 4 hours; received amiplatelin within 48 hours (if ischemic); and underwent physiotherapist, nutrition, and formal swallow assessments within 72 hours (all if eligible).

Statistical Analysis
Descriptive Statistics
Descriptive data were calculated at regional level for Greater Manchester, London, and the comparator, pre- and postcentralization. Postcentralization, we categorized hospitals based on whether they were designated to provide hyperacute care. Consistent data were available on patient characteristics (age, sex, stroke type, worst level of consciousness, and whether the stroke occurred within or outside hospital) and the proportion of patients receiving each clinical intervention analysed.

Hospital-Level Variation
To understand the impact of the centralizations on patient volume and provision of care at hospital level, the unadjusted proportion of patients receiving evidence-based clinical interventions was calculated at hospital level for each area, pre- and postcentralization. Hospital-level proportions were plotted against the mean number of stroke patients submitted to the audits per day and categorized by whether services were hyperacute.

Risk-Adjusted Likelihood of Receiving Evidence-Based Clinical Interventions
Using patient-level data, we used logistic regression to analyze whether patients received each evidence-based clinical intervention (yes/no) against region (whether they were treated in Greater Manchester or London [with the comparator as the reference category]), time period (whether they were treated in the after period [with being treated in the before period as the reference category]), and an interaction term between region and time period, controlling for age (in 5 year bands), sex, stroke diagnosis (intracerebral hemorrhage/cerebral infarction), worst level of consciousness (fully conscious/semi-conscious/drowsy/unconscious), and whether stroke occurred within or outside hospital (yes/no). All outcomes were binary (yes/no). We report marginal effects showing the adjusted predicted probability of each outcome in each region in each time period. Because the Greater Manchester and London centralizations had different after periods (meaning the comparator data differed slightly), the regression analyses of the 2 centralizations were conducted separately. We reran our models stratifying by whether the patient was treated in a hyperacute or a nonhyperacute stroke service.

Following Referral Criteria for Admission to Hyperacute Units in Greater Manchester and London
The proportion of patients treated in a hyperacute stroke unit was calculated to examine whether the models selected in Greater Manchester and London influenced the likelihood of receiving evidence-based clinical interventions; this was also used to measure how reliably the London hyperacute referral criteria were followed. To examine how reliably Greater Manchester hyperacute referral criteria were followed, we compared patients’ time of symptom onset with time of arrival at hospital to calculate the proportion of patients who arrived at hospital within 4 hours of symptoms developing (and were thus eligible for hyperacute unit admission) and who were in fact admitted to a hyperacute unit.

Ethical Approval
This study received ethical approval in September 2011 from the London East National Health Service (NHS) Research Ethics Committee (Ref 11/LO/1396).

Results
Descriptive Statistics
Data for 38,623 acute stroke cases submitted to national audit were analyzed, covering 51 hospitals precentralization (from a total of 189 hospitals participating in the audit across England) and 44 hospitals postcentralization (from a total of 171 hospitals across England). Table 1 presents unadjusted data for Greater Manchester and London compared with the comparator. Patient characteristics were similar in Greater Manchester, London, and the comparator in both pre- and postcentralization time periods, and any potential effects of patient characteristics were controlled for in the regression analyses. Postcentralization, the proportion of patients receiving evidence-based clinical interventions increased in all 3 areas. It should be noted that denominators for these indicators varied from measure to measure because of variable eligibility of patients or availability of data. Increases were most pronounced in care provided in the first hours following arrival at hospital (brain scan within 3 hours, admitted to stroke unit within 4 hours). The proportion of stroke patients receiving these clinical interventions was higher in London than in Greater Manchester and the comparator, both pre- and postcentralization, but the absolute difference was similar. Proportions of patients receiving evidence-based clinical interventions 24 to 72 hours after admission also increased in all 3 areas, but in all areas precentralization levels commonly exceeded 80% and postcentralization all proportions exceeded 90%. Generally, London had higher precentralization levels, and postcentralization levels were similar—approaching the maximum—in each area.

Hospital-Level Variation
Precentralization, there was substantial between-hospital variation in the proportion of patients receiving evidence-based clinical interventions in all 3 areas (Figure 2; online-only Data Supplement). Postcentralization, hyperacute units in Greater Manchester (Comprehensive Stroke Center, PSCs) and London (HASUs) treated a higher volume of patients than elsewhere (Table 1) and provided evidence-based clinical interventions to a higher proportion of their patients (Figure 3; and online-only Data Supplement).
Although the proportion of patients receiving evidence-based clinical interventions increased in Greater Manchester and London’s non-hyperacute units and in the comparator area overall, patient volume increased less, and the proportion of patients receiving evidence-based clinical interventions tended to be lower and more variable than in the hyperacute units. When Greater Manchester PSCs operated as DSCs, they performed in line with other DSCs (Figure 3A).

**Risk-Adjusted Likelihood of Receiving Evidence-Based Clinical Interventions**

Trends in risk-adjusted proportions of patients receiving evidence-based clinical interventions reflect the unadjusted findings (Tables 2 and 3). Postcentralization, on all clinical interventions analyzed, London patients were overall significantly more likely to receive clinical interventions than comparator patients. Greater Manchester patients were significantly more likely than comparator patients to receive 2 interventions (brain scan within 3 and 24 hours), significantly less likely to receive 3 interventions (admission to stroke unit within 4 hours and physiotherapist and swallow assessments within 72 hours), with no significant difference between Greater Manchester and comparator patients on the 2 remaining interventions. London patients were overall significantly more likely than Greater Manchester patients to receive 6 of the 7 interventions (brain scan within 3 and 24 hours, admission to stroke unit within 4 hours, and physiotherapist, nutrition, and swallow assessments within 72 hours, postcentralization).
hours, with magnitude of differences ranging from 1.2% to 10.4%, with no significant difference on antiplatelet within 48 hours). Patients treated in hyperacute units, in both Greater Manchester and London, were significantly more likely to receive clinical interventions than patients treated either in nonhyperacute units or in the comparator (with one exception, where comparator patients were significantly more likely to receive physiotherapist assessment than Greater Manchester
hyperacute patients). Patients treated in Greater Manchester hyperacute units were significantly more likely than London HASU patients to receive 4 clinical interventions: brain scan within 3 hours, admission to stroke unit within 4 hours, brain scan within 24 hours, and antiplatelet within 48 hours (the magnitude of the differences ranged from 2.0% to 13.8%). Patients treated in Greater Manchester hyperacute units were significantly less likely to receive physiotherapist assessment within 72 hours than patients treated in London HASUs (magnitude 2.2%). There was no significant difference between Greater Manchester and London hyperacute units on patients receiving nutrition and formal swallow assessments within 72 hours. To examine whether these differences reflected the greater proportion of patients in Greater Manchester arriving within 4 hours, we reran this analysis focusing only on patients presenting within 4 hours of symptom onset and found the differences between Greater Manchester and London hyperacute units reduced substantially (see online-only Data Supplement).

### Access to Care in Hyperacute Units in Greater Manchester and London

Postcentralization, while 39% of Greater Manchester patients were treated in a hyperacute unit, 93% of London patients were treated in a hyperacute unit (Table 1). This is explained in part by the different eligibility criteria for admission to hyperacute units in Greater Manchester and London. However, in addition, only 66% of Greater Manchester stroke patients who presented within 4 hours of symptom onset were admitted to a hyperacute unit (Table 1), meaning 34% of patients who were eligible for hyperacute unit care were not admitted to one. This result was in line with an analysis conducted by the Greater Manchester and Cheshire Cardiac and Stroke Network as part of their 12-month review of the centralization.11

We reran our analyses using all available data for the rest of England as the comparator: the results did not change appreciably (see online-only Data Supplement).

### Discussion

Postcentralization, risk-adjusted likelihood of patients receiving evidence-based clinical interventions increased significantly in all areas. London patients were overall significantly more likely than patients elsewhere to receive the interventions. Importantly, hyperacute units in both Greater Manchester and London were significantly more likely to provide interventions than nonhyperacute units in these areas and in the comparator area overall.

Fewer than 40% of Greater Manchester patients were admitted to a hyperacute unit, whereas 93% of London patients were: this is likely to explain the overall differences in provision over the 2 areas and suggests a clear effect of

### Table 2. Risk-Adjusted Proportions of Patients Receiving Evidence-Based Clinical Interventions: Greater Manchester Versus Comparator

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Overall</th>
<th>CSC/PSCs</th>
<th>DSCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain scan 3 h</td>
<td>25.0% [21.0–29.0]</td>
<td>65.2% [64.3–66.2]</td>
<td>85.5% [84.6–86.5]</td>
</tr>
<tr>
<td>Stroke Unit 4 h</td>
<td>17.8% [14.6–21.0]</td>
<td>55.9% [54.9–57.0]</td>
<td>82.9% [81.8–83.9]</td>
</tr>
<tr>
<td>Brain scan 24 h</td>
<td>71.7% [68.2–75.1]</td>
<td>94.0% [93.5–94.4]</td>
<td>98.2% [97.8–98.5]</td>
</tr>
<tr>
<td>Antiplatelet 48 h</td>
<td>86.5% [83.8–89.2]</td>
<td>94.2% [93.7–94.7]</td>
<td>97.6% [97.1–98.1]</td>
</tr>
<tr>
<td>Physio 72 h</td>
<td>88.3% [85.7–90.8]</td>
<td>92.1% [91.5–92.7]</td>
<td>93.8% [93.0–94.7]</td>
</tr>
<tr>
<td>Nutrition 72 h</td>
<td>89.9% [87.7–92.0]</td>
<td>95.6% [95.3–96.0]</td>
<td>98.5% [98.2–98.8]</td>
</tr>
<tr>
<td>Swallow 72 h</td>
<td>87.7% [84.6–90.9]</td>
<td>94.0% [93.6–94.4]</td>
<td>98.6% [98.2–98.9]</td>
</tr>
</tbody>
</table>

### Table 3. Risk-Adjusted Proportions of Patients Receiving Evidence-Based Clinical Interventions: London Versus Comparator

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Overall</th>
<th>HASUs</th>
<th>SU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain scan 3 h</td>
<td>36.5% [34.0–39.1]</td>
<td>72.1% [71.4–72.8]</td>
<td>74.6% [73.8–75.3]</td>
</tr>
<tr>
<td>Stroke Unit 4 h</td>
<td>29.6% [27.3–31.9]</td>
<td>66.3% [65.6–67.1]</td>
<td>69.1% [68.3–69.9]</td>
</tr>
<tr>
<td>Brain scan 24 h</td>
<td>77.9% [75.8–80.0]</td>
<td>95.2% [94.8–95.5]</td>
<td>96.2% [95.9–96.5]</td>
</tr>
<tr>
<td>Antiplatelet 48 h</td>
<td>94.1% [92.8–95.4]</td>
<td>94.8% [94.4–95.2]</td>
<td>95.3% [94.9–95.7]</td>
</tr>
<tr>
<td>Physio 72 h</td>
<td>88.9% [87.0–90.7]</td>
<td>95.4% [95.0–95.8]</td>
<td>96.0% [95.6–96.4]</td>
</tr>
<tr>
<td>Nutrition 72 h</td>
<td>74.1% [71.7–76.4]</td>
<td>98.3% [98.1–98.5]</td>
<td>98.6% [98.4–98.8]</td>
</tr>
<tr>
<td>Swallow 72 h</td>
<td>85.4% [82.8–88.0]</td>
<td>98.2% [97.9–98.4]</td>
<td>99.0% [98.8–99.1]</td>
</tr>
</tbody>
</table>

HASU indicates Hyperacute Stroke Units; and SU, Stroke Unit.
the models selected. This effect partly relates to the different eligibility criteria for admission to hyperacute unit: in Greater Manchester, only stroke patients presenting within 4 hours of developing symptoms were eligible, whereas all London stroke patients were. However, in Greater Manchester, only two thirds of patients eligible for care in a hyperacute unit were admitted to one; this suggests that differences between Greater Manchester and London derived not only from the eligibility criteria, but also from how reliably they were followed, with both contributing to the lower overall likelihood of patients receiving interventions in Greater Manchester. The fact that Greater Manchester hyperacute units were significantly more likely than London HASUs to provide 4 of the interventions analyzed may relate to the ways in which London and Greater Manchester hyperacute units were designed and specified (eg, in terms of staffing and availability of allied services, Greater Manchester’s use of the 4 hour eligibility criterion, and the extent to which services had to operate a 24/7 service) and how these specifications were implemented. The contrast in performance by PSCs in hours and out of hours is likely to reflect the differing specifications for hyperacute and nonhyperacute services applied at these times, including staffing levels and access to diagnostic services. In both areas, nonhyperacute units were less likely to provide interventions, reflecting an important consideration when centralizing services. In London, only 7% of London patients were treated in SUs: this had a negligible effect, but may reflect issues where the referral protocol was not followed. In Greater Manchester, DSCs were less likely to provide the interventions analyzed; as DSCs treated 61% of Greater Manchester patients, Greater Manchester and comparator services performed similarly overall, suggesting the benefits of this centralization were limited. It should be noted that, to address these issues, Greater Manchester recently centralized its services further, implementing a model more in line with the one used in London and originally planned in Greater Manchester. Finally, it is unlikely that geography influenced Greater Manchester patient eligibility significantly, given that the maximum distance from any point in Greater Manchester to the 24/7 Comprehensive Stroke Center is <25 miles.

Little is known about how large scale service centralization influences provision of evidence-based stroke clinical interventions, but there is substantial evidence that such clinical interventions are associated with better clinical outcomes, for example, through dedicated stroke units with specialist staff providing rapid assessment, treatment, and therapies.1,2,17–19 Recent research indicates that the London centralization had a significantly greater impact on patient mortality than in the rest of England, whereas the Greater Manchester centralization did not.4 The current analysis suggests that this difference might result from better access (on average) to evidence-based clinical interventions on arrival at hospital in London because of a higher proportion of patients being admitted to hyperacute units. This in turn suggests the model implemented is important: centralizing acute stroke services into a small number of hyperacute units can increase access to evidence-based clinical interventions, which may in turn lead to better clinical outcomes. Further, the model selected may influence the extent to which it is followed: the Greater Manchester model may have been followed less reliably because of complexity associated with the 4-hour eligibility criterion for admission to hyperacute units and PSCs’ limited hours. This in turn suggests potential advantages to service models that aim for relative simplicity. Therefore, our findings indicate that there may be significant benefits in models where all stroke patients are eligible for hyperacute unit admission: offering hyperacute unit admission selectively, for example, based on time of stroke onset, may limit these benefits. As the centralizations studied were implemented in large metropolitan areas, these findings are of greatest relevance to urban settings.

General increases in likelihood of patients receiving interventions, reflected in the comparator, should also be noted. These may reflect the influence of national drivers to improve stroke care across England, for example, the National Stroke Strategy13 and the “Stroke Best Practice Tariff”,20,21 increasing hospitals’ prioritization of clinical interventions measured in national stroke audits. This may contribute to the overall lower likelihood of Greater Manchester patients undergoing 4 of the interventions than comparator patients because our data indicate comparatively limited improvements in DSC services, whereas general improvements occurred in many of the comparator services.

To study the impact of centralizing acute stroke services, we have been able to analyze 2 different models of centralization implemented within the same national healthcare system at approximately the same time using data from 2 comprehensive national audits. This allowed us to compare findings between the 2 centralizations and with a large, urban comparator, thus enhancing external validity. Our study has several limitations. First, because of variable participation in SINAP, it was not appropriate to use the rest of England as our comparator; this limits the extent to which we may use these results to explain previous research on the impact of these centralizations on mortality. Second, it is possible that data completeness may have varied across hospitals in the Greater Manchester, London, and comparator areas, thus limiting the confidence with which we interpret the data analyzed. Third, because of data availability, several important clinical interventions could not be analyzed. Provision and timing of thrombolysis were excluded because in 2008 thrombolysis rates were not reported with sufficient frequency to permit reliable analysis. However, the stroke services analysed aim to treat all stroke patients, only a proportion of whom (≈16%)22 are eligible for thrombolysis. Other interventions excluded were anticoagulation of atrial fibrillation (data were not collected in either audit) and occupational therapy assessment and continence assessment (criteria assessed changed over time). Fourth, it was not possible to adjust for stroke severity (eg, using the National Institutes of Health Stroke Scale) because these data were not collected in either audit analyzed. However, it is recommended that stroke patients receive these interventions regardless of severity (unless contraindicated); therefore, controlling for severity should have little impact on whether these interventions are provided. However, the latest version of the audit collects National Institutes of Health Stroke Scale for all patients on arrival at hospital, and future research might usefully analyze
whether stroke severity influences likelihood of receiving interventions. Fifth, because the areas studied varied in overall performance levels precentralization and several of the selected indicators approached ceiling both pre- and postcentralization, our analysis of change over time was limited. Sixth, it was not possible to control for hospital/unit effects because the number and function of stroke services changed significantly over the period studied. Finally, the analysis of patients presenting within 4 hours of their symptoms appearing was derived from SINAP data on time of stroke symptom onset: although we made every effort to exclude unreliable data, it remains that some may have been recorded unreliably.

Our data indicate both that the centralization model selected and the degree to which it was followed may have influenced the likelihood of stroke patients receiving evidence-based clinical interventions and that these factors may be interrelated. Therefore, qualitative analysis of how model selection and implementation processes influenced the development of hyperacute and nonhyperacute services, and the reliability with which patients were transferred to these services, is required to generate valuable lessons for future changes of this kind. Future research should analyze the impact of centralization on such outcomes as patient and carer experience, poststroke independence, disability, and quality of life. Finally, the cost and cost effectiveness of centralization should also be explored.

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Disclosures

References
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SUPPLEMENTAL MATERIAL

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Note. All analyses reported in this online supplement in relation to provision of evidence-based clinical interventions present data for patients who were eligible for these interventions (eligibility outlined in national reports for Sentinel 2008\(^1\) and SINAP\(^2\))
SUPPLEMENTAL METHODS

Process of selecting the comparator area

Table I presents participation in Sentinel 2008 (pre-centralization) and SINAP (post-centralization), organized by area (Greater Manchester, London, rest of England).

Table I. Proportion of participating sites, by area and phase

<table>
<thead>
<tr>
<th>Region</th>
<th>Proportion of sites participating in Sentinel 2008 (%)</th>
<th>Proportion of sites participating in SINAP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater Manchester</td>
<td>12/12 (100%)</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>London</td>
<td>30/30 (100%)</td>
<td>24/24 (100%)</td>
</tr>
<tr>
<td>Rest of England</td>
<td>147/147 (100%)</td>
<td>96/136 (70.6%)</td>
</tr>
</tbody>
</table>

Sentinel 2008 had high levels of participation across all regions of England: it was estimated that all acute trusts admitting acute stroke patients took part in the audit. In SINAP, the proportion of sites participating across the Rest of England was considerably lower than in London and Greater Manchester. Given the different levels of participation in the before and after periods, we concluded that the rest of England would not represent a suitable control group for a before and after analysis.

Table II presents participation in SINAP by region, in terms of 1) number of cases submitted to SINAP per head of local population and 2) the proportion of organisations submitting data to SINAP

Table II. Numbers of cases submitted to SINAP by Region of England

<table>
<thead>
<tr>
<th>Region</th>
<th>Population 2011</th>
<th>Total cases submitted</th>
<th>Cases per 100000</th>
<th>Proportion of sites participating (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. East Midlands</td>
<td>4533222</td>
<td>3040</td>
<td>67.06</td>
<td>4/10 (40%)</td>
</tr>
<tr>
<td>2. East of England</td>
<td>5846965</td>
<td>4261</td>
<td>72.88</td>
<td>11/17 (64.71%)</td>
</tr>
<tr>
<td>3. London</td>
<td>8173941</td>
<td>16773</td>
<td>205.20</td>
<td>24/24 (100%)</td>
</tr>
<tr>
<td>4. North East</td>
<td>2596886</td>
<td>7877</td>
<td>303.32</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>5. North West</td>
<td>7052177</td>
<td>24350</td>
<td>345.28</td>
<td>24/27 (100%)</td>
</tr>
<tr>
<td>5a. Greater Manchester</td>
<td>2682500</td>
<td>10295</td>
<td>383.78</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>5b. Rest of North West England</td>
<td>4369677</td>
<td>14055</td>
<td>321.65</td>
<td>16/16 (100%)</td>
</tr>
<tr>
<td>6. South East England</td>
<td>8634750</td>
<td>8813</td>
<td>102.06</td>
<td>19/28 (67.86%)</td>
</tr>
<tr>
<td>7. South West</td>
<td>5288935</td>
<td>7431</td>
<td>140.50</td>
<td>8/18 (44.44%)</td>
</tr>
<tr>
<td>8. West Midlands</td>
<td>5601847</td>
<td>5659</td>
<td>101.02</td>
<td>16/20 (80%)</td>
</tr>
<tr>
<td>9. Yorkshire and the Humber</td>
<td>5283733</td>
<td>6680</td>
<td>126.43</td>
<td>11/16 (68.75%)</td>
</tr>
<tr>
<td>England (total)</td>
<td>53012456</td>
<td>84884</td>
<td>160.12</td>
<td>131/171 (76.6%)</td>
</tr>
</tbody>
</table>

Note. Population figures were drawn from 2011 UK census data. Total numbers of cases submitted were drawn from our analysis. Proportion of sites participating: the numerator was drawn from our analysis, and the denominator from publicly reported SINAP data. In line with our analysis, we report all 24 London sites submitting data to SINAP.

This analysis shows that Greater Manchester and London had high levels of participation on both selected criteria, and well above the average for England. The only other areas with similar levels of participation were North East England and the rest of North West England (i.e. excluding Greater Manchester). Based on this analysis it was decided that the data from these areas should be used as the control group in both the pre- and post-centralization periods of the analyses, with data from other areas excluded.

To ensure comparability with Greater Manchester and London, both of cover areas classified by the United Kingdom’s Office for National Statistics as ‘major urban’ (“districts with either 100,000 people or 50% of their population in urban areas with a population of more than 750,000”)5, we limited services in the comparator to those serving populations classified by
the ONS as ‘major urban’. This was done by mapping locations of each service in the comparator and selecting those in districts classified as ‘major urban’. Details of cases included and excluded from the analysis are presented in table III.

**Table III. Summary of inclusion and exclusion of stroke cases in this analysis**

<table>
<thead>
<tr>
<th></th>
<th>Sentinel 2008</th>
<th>SINAP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater Manchester</td>
<td>653</td>
<td>10,295</td>
<td>10,948</td>
</tr>
<tr>
<td>London</td>
<td>1,541</td>
<td>16,773</td>
<td>18,314</td>
</tr>
<tr>
<td>Urban comparator</td>
<td>537</td>
<td>9,044</td>
<td>9,581</td>
</tr>
<tr>
<td>Excluded cases</td>
<td>7,341</td>
<td>48,772</td>
<td>56,113</td>
</tr>
<tr>
<td>Total cases</td>
<td>10,072</td>
<td>84,884</td>
<td>94,956</td>
</tr>
</tbody>
</table>

**References**

SUPPLEMENTAL TABLES

Risk-adjusted analyses with rest of England data acting as comparator

Table III. Risk-adjusted proportions of patients receiving evidence-based clinical interventions: Greater Manchester versus rest of England

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Greater Manchester (% likelihood (95% confidence intervals))</th>
<th>Rest of England</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Before</td>
</tr>
<tr>
<td>Brain scan 3h</td>
<td>21.2%</td>
<td>60.9%</td>
</tr>
<tr>
<td>Stroke Unit 4h</td>
<td>15.9%</td>
<td>53.1%</td>
</tr>
<tr>
<td>Brain scan 24h</td>
<td>68.2%</td>
<td>93.0%</td>
</tr>
<tr>
<td>Antiplatelet 48h</td>
<td>86.5%</td>
<td>93.9%</td>
</tr>
<tr>
<td>Physio 72h</td>
<td>88.0%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Nutrition 72h</td>
<td>88.2%</td>
<td>94.9%</td>
</tr>
<tr>
<td>Swallow 72h</td>
<td>85.6%</td>
<td>92.7%</td>
</tr>
</tbody>
</table>

Note: Patients treated in hospitals hosting PSCs only classed as being treated in hyperacute unit if arriving between 7am and 7pm, Monday - Friday; out of hours, these patients classed as being treated in a DSC.

Table IV. Risk-adjusted proportions of patients receiving evidence-based clinical interventions: London versus rest of England

<table>
<thead>
<tr>
<th>Indicator</th>
<th>London (% likelihood [95% confidence intervals])</th>
<th>Rest of England</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Before</td>
</tr>
<tr>
<td>Brain scan 3h</td>
<td>36.1%</td>
<td>72.0%</td>
</tr>
<tr>
<td>Stroke Unit 4h</td>
<td>30.8%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Brain scan 24h</td>
<td>77.1%</td>
<td>96.1%</td>
</tr>
<tr>
<td>Antiplatelet 48h</td>
<td>94.2%</td>
<td>95.4%</td>
</tr>
<tr>
<td>Physio 72h</td>
<td>90.4%</td>
<td>96.6%</td>
</tr>
<tr>
<td>Nutrition 72h</td>
<td>74.6%</td>
<td>98.4%</td>
</tr>
<tr>
<td>Swallow 72h</td>
<td>87.3%</td>
<td>98.4%</td>
</tr>
</tbody>
</table>
**SUPPLEMENTAL TABLES**

**Risk-adjusted analysis of impact of following referral protocol in Greater Manchester**

Table V. Risk-adjusted proportions of Greater Manchester DSC patients receiving evidence-based clinical interventions, depending on whether admitted within or beyond 4 hours after onset of symptoms

<table>
<thead>
<tr>
<th>Intervention</th>
<th>CSC/PScs after</th>
<th>DSCs after (% likelihood [95% confidence intervals])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Overall (where onset time available)</td>
</tr>
<tr>
<td>Brain scan 3h</td>
<td>84.6% (83.6-85.6)</td>
<td>50.7% [49.4-51.9]</td>
</tr>
<tr>
<td>Stroke Unit 4h</td>
<td>81.4% (80.3-82.5)</td>
<td>34.1% [32.8-35.4]</td>
</tr>
<tr>
<td>Brain scan 24h</td>
<td>98.0% (97.6-98.4)</td>
<td>90.9% [90.2-91.5]</td>
</tr>
<tr>
<td>Antiplatelet 48h</td>
<td>97.6% (97.1-98.1)</td>
<td>92.1% [91.4-92.8]</td>
</tr>
<tr>
<td>Physio 72h</td>
<td>93.5% (92.7-94.4)</td>
<td>91.1% [90.4-91.8]</td>
</tr>
<tr>
<td>Nutrition 72h</td>
<td>98.3% (97.9-98.6)</td>
<td>93.3% [92.8-93.9]</td>
</tr>
<tr>
<td>Swallow 72h</td>
<td>98.2% (97.9-98.6)</td>
<td>90.1% [89.4-90.8]</td>
</tr>
</tbody>
</table>
### SUPPLEMENTAL TABLES

**Risk adjusted analysis of impact of time of arrival at hyperacute unit in Greater Manchester and London**

Table VI. Risk-adjusted proportions of London HASU patients receiving evidence-based clinical interventions, depending on whether admitted within or beyond 4 hours after onset of symptoms

<table>
<thead>
<tr>
<th>Indicator</th>
<th>HASUs - after (% likelihood [95% confidence intervals])</th>
<th>≤4h</th>
<th>&gt;4h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>≤4h</td>
<td>&gt;4h</td>
</tr>
<tr>
<td>Brain scan 3h</td>
<td>74.6% [73.8-75.3]</td>
<td>91.4% [90.6-92.2]</td>
<td>68.7% [67.1-70.2]</td>
</tr>
<tr>
<td>Stroke Unit 4h</td>
<td>69.1% [68.3-69.9]</td>
<td>80.1% [79.8-82.0]</td>
<td>64.7% [63.0-66.3]</td>
</tr>
<tr>
<td>Brain scan 24h</td>
<td>96.2% [95.9-96.5]</td>
<td>98.9% [98.6-99.1]</td>
<td>96.4% [95.7-97.0]</td>
</tr>
<tr>
<td>Antiplalet 48h</td>
<td>95.3% [94.9-95.7]</td>
<td>94.9% [94.2-95.6]</td>
<td>96.4% [95.7-97.1]</td>
</tr>
<tr>
<td>Physio 72h</td>
<td>96.0% [95.6-96.4]</td>
<td>95.6% [94.9-96.3]</td>
<td>96.1% [95.3-97.0]</td>
</tr>
<tr>
<td>Nutrition 72h</td>
<td>98.6% [98.4-98.8]</td>
<td>98.7% [98.3-99.0]</td>
<td>99.0% [98.6-99.3]</td>
</tr>
<tr>
<td>Swallow 72h</td>
<td>99.0% [98.8-99.1]</td>
<td>99.2% [98.9-99.5]</td>
<td>99.2% [98.8-99.5]</td>
</tr>
</tbody>
</table>

Table VII. Risk-adjusted proportions of Greater Manchester CSC/PSC patients receiving evidence-based clinical interventions, depending on whether admitted within or beyond 4 hours after onset of symptoms

<table>
<thead>
<tr>
<th>Indicator</th>
<th>CSC/PSC - after (% likelihood [95% confidence intervals])</th>
<th>≤4h</th>
<th>&gt;4h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>≤4h</td>
<td>&gt;4h</td>
</tr>
<tr>
<td>Brain scan 3h</td>
<td>85.5% [84.6-86.5]</td>
<td>92.7% [91.7-93.7]</td>
<td>83.1% [80.9-85.2]</td>
</tr>
<tr>
<td>Stroke Unit 4h</td>
<td>82.9% [81.8-83.9]</td>
<td>90.1% [89.1-91.3]</td>
<td>83.5% [81.3-85.6]</td>
</tr>
<tr>
<td>Brain scan 24h</td>
<td>98.2% [97.8-98.5]</td>
<td>99.4% [99.1-99.7]</td>
<td>98.2% [97.5-99.1]</td>
</tr>
<tr>
<td>Antiplalet 48h</td>
<td>97.6% [97.1-98.1]</td>
<td>98.3% [97.7-98.9]</td>
<td>98.2% [97.3-99.1]</td>
</tr>
<tr>
<td>Physio 72h</td>
<td>93.8% [93.0-94.7]</td>
<td>93.4% [92.1-94.6]</td>
<td>95.6% [94.2-97.1]</td>
</tr>
<tr>
<td>Nutrition 72h</td>
<td>98.5% [98.2-98.8]</td>
<td>98.9% [98.5-99.2]</td>
<td>98.5% [97.9-99.2]</td>
</tr>
<tr>
<td>Swallow 72h</td>
<td>98.6% [98.2-98.9]</td>
<td>99.3% [99.0-99.6]</td>
<td>98.5% [98.0-99.2]</td>
</tr>
</tbody>
</table>

Note. Overall figures drawn from full dataset, whereas ≤4h and >4h figures based on data where reliable symptom onset data were available.
SUPPLEMENTAL FIGURES

Between-hospital variations by area (Greater Manchester, London, Comparator, rest of England), before and after centralization

Overview:

**Figures I-IV**: Proportion of patients undergoing brain scan within 3 hours

**Figures V-VIII**: Proportion of patients admitted to stroke unit within 4 hours

**Figures IX-XII**: Proportion of patients undergoing brain scan within 24 hours

**Figures XIII-XVI**: Proportion of patients administered antiplatelet within 48 hours

**Figures XVII-XX**: Proportion of patients receiving physiotherapist assessment within 72 hours

**Figures XXI-XXIV**: Proportion of patients receiving nutrition assessment within 72 hours

**Figures XXV-XXVIII**: Proportion of patients receiving swallow assessment within 72 hours
Figure I. Proportion of patients undergoing brain scan within 3 hours: Greater Manchester
A) Pre-centralization  
B) Post-centralization

Figure II. Proportion of patients undergoing brain scan within 3 hours: London
A) Pre-centralization  
B) Post-centralization

Figure III. Proportion of patients undergoing brain scan within 3 hours: Comparator
A) Pre-centralization  
B) Post-centralization

Figure IV. Proportion of patients undergoing brain scan within 3 hours: rest of England
A) Pre-centralization  
B) Post-centralization
Figure V. Proportion of patients admitted to stroke unit within 4 hours: Greater Manchester
A) Pre-centralization
B) Post-centralization

Figure VI. Proportion of patients admitted to stroke unit within 4 hours: London
A) Pre-centralization
B) Post-centralization

Figure VII. Proportion of patients admitted to stroke unit within 4 hours: Comparator
A) Pre-centralization
B) Post-centralization

Figure VIII. Proportion of patients admitted to stroke unit within 4 hours: Rest of England
A) Pre-centralization
B) Post-centralization
Figure IX. Proportion of patients undergoing brain scan within 24 hours: Greater Manchester
A) Pre-centralization

B) Post-centralization

Figure X. Proportion of patients undergoing brain scan within 24 hours: London
A) Pre-centralization

B) Post-centralization

Figure XI. Proportion of patients undergoing brain scan within 24 hours: Comparator
A) Pre-centralization

B) Post-centralization

Figure XII. Proportion of patients undergoing brain scan within 24 hours: Rest of England
A) Pre-centralization

B) Post-centralization
Figure XIII. Proportion of patients administered antiplatelet within 48 hours: Greater Manchester
A) Pre-centralization

Figure XIV. Proportion of patients administered antiplatelet within 48 hours: London
A) Pre-centralization

Figure XV. Proportion of patients administered antiplatelet within 48 hours: Comparator
A) Pre-centralization

Figure XVI. Proportion of patients administered antiplatelet within 48 hours: Rest of England
A) Pre-centralization
Figure XVII. Proportion of patients receiving physiotherapist assessment within 72 hours: Greater Manchester
A) Pre-centralization

Figure XVIII. Proportion of patients receiving physiotherapist assessment within 72 hours: London
A) Pre-centralization

Figure XIX. Proportion of patients receiving physiotherapist assessment within 72 hours: Comparator
A) Pre-centralization

Figure XX. Proportion of patients receiving physiotherapist assessment within 72 hours: rest of England
A) Pre-centralization
Figure XXI. Proportion of patients receiving nutrition assessment within 72 hours: Greater Manchester
A) Pre-centralization  
B) Post-centralization

Figure XXII. Proportion of patients receiving nutrition assessment within 72 hours: London
A) Pre-centralization  
B) Post-centralization

Figure XXIII. Proportion of patients receiving nutrition assessment within 72 hours: Comparator
A) Pre-centralization  
B) Post-centralization

Figure XXIV. Proportion of patients receiving nutrition assessment within 72 hours: rest of England
A) Pre-centralization  
B) Post-centralization
Figure XXV. Proportion of patients receiving swallow assessment within 72 hours: Greater Manchester
A) Pre-centralization  
B) Post-centralization

Figure XXVI. Proportion of patients receiving swallow assessment within 72 hours: London
A) Pre-centralization  
B) Post-centralization

Figure XXVII. Proportion of patients receiving swallow assessment within 72 hours: Comparator
A) Pre-centralization  
B) Post-centralization

Figure XXVIII. Proportion of patients receiving swallow assessment within 72 hours: rest of England
A) Pre-centralization  
B) Post-centralization