

# Protocol for an observation and implementation study investigating optimisation of the management of stroke and transient ischaemic attack (TIA)

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## ABSTRACT

**Introduction:** Patients benefit from early and intensive treatment in both acute ischaemic stroke and transient ischaemic attack. Recent audits of acute stroke/transient ischaemic attack care suggest that although standards have improved, current services still fall short of optimal care. The aim of this study is to establish a database of patients accessing stroke services. Data will be collected and analysed to provide individualised feedback to healthcare professionals who can then use these findings to develop strategies for service improvement.

**Methods and analysis:** This longitudinal observational study will evolve with the ongoing findings from the research output. The project will consist of three phases: assessment of current practice, feedback of findings and evaluation of service change. Consecutive patients will be recruited from participating hospitals, and identifiable data will be collected to link records from the Primary Care, Secondary Care and Emergency Services. As this study focuses on observation of current practice, a sample size calculation is not deemed appropriate. Patients will be sent follow-up questionnaires examining quality of life at 3 and 12 months post-event. Qualitative interviews will examine the care pathway through the experiences of patients, their carers, healthcare personnel and commissioners. Collected data will be used in economic analyses, which will evaluate the impact of current care and service redesign on the NHS costs and patient outcomes (death and quality of life).

**Ethics and dissemination:** Ethical approval for this study has been obtained from the National Research Ethics Committee (reference; 09/H0716/71), and site-specific R&D approval has been acquired from the relevant NHS trusts. All findings will be presented at relevant healthcare/academic conferences and written up for publication in peer-reviewed journals. Results will be fed back to patients and participating trusts through a series of reports and presentations. These

## ARTICLE SUMMARY

### Article focus

- Optimising the management of stroke and transient ischaemic attack (TIA).
- Study protocol using a mixed-methods approach.

### Key messages

- Stroke and TIA are not currently managed effectively across the care pathway.
- This project will collect patient data across the care pathway from multiple NHS trusts.
- A model of research, feedback and evaluation will be adopted.

### Strengths and limitations of this study

- Combining data collection from multiple health-care settings with economic evaluations will provide a unique insight into stroke and TIA management across the care pathway.
- The need to obtain informed consent from patients to allow data linkage may limit the completeness of the data.

will be used to facilitate discussions about service redesign and implementation.

## BACKGROUND

Stroke is one of the leading causes of morbidity and mortality worldwide, with an estimated 5.7 million deaths and 50 million disability-adjusted life-years lost every year.<sup>1</sup> To this end, stroke-related mortality is expected to rise by 37% in the next 20 years.<sup>1</sup> Effective diagnosis and management of stroke and transient ischaemic attack (TIA) is therefore of importance.

It is now well recognised that people who have a stroke or TIA benefit from early

intensive treatment: in acute ischaemic stroke, thrombolysis within 3 h of symptom onset results in improved outcomes<sup>2</sup> and has thus been recommended by the National Institute for Health and Clinical Excellence.<sup>3</sup> Indeed, this has now been extended to 4.5 h following observational data suggesting benefit from thrombolysis past the original time window.<sup>4</sup> Similarly, people having a TIA are at high risk of having a subsequent stroke; these risks are highest in the first few days following the event.<sup>5</sup> There are several interventions, both medical and surgical, that can substantially reduce this risk of stroke following a TIA, and evidence that earlier intervention is better.<sup>6</sup>

To ensure that patients with stroke and TIA receive diagnosis and treatment quickly, national guidelines recommend that services be designed to include a combination of emergency referral, early brain imaging and thrombolysis in acute stroke and immediate referral for urgent specialist assessment and investigation in TIA.<sup>6-7</sup> The National Sentinel Stroke Audit reveals that although standards have improved, current care still falls short of these aspirations: in 2010, only 5% of patients received thrombolysis for acute stroke.<sup>8</sup> For TIA services, care has improved with specialist review following TIA occurring within 7 days in 97% of high-risk patients and 86% of low-risk patients.<sup>9</sup> However, this still falls short of the 100% specified in clinical guidelines.

The National Sentinel Stroke Audit<sup>8</sup> is a useful tool for assessing current hospital stroke services across the country. However, this includes a small proportion of the total patients and cannot assess the whole care pathway for patients with acute stroke and TIA. Pre- and post-event management in Primary Care and via Emergency Services may have a significant impact on stroke and other cardiovascular events,<sup>10</sup> hence effective pre-hospital care is vital in achieving the standards set out in the National Stroke Strategy.<sup>7</sup> Currently, it is not clear to what extent the interaction between services impacts patient care and outcomes.

The aim of this project is to identify barriers to effective treatments and model the impact of service change on patient outcomes and NHS costs using data collected from the Primary Care, Secondary Care and Emergency Services. In addition, qualitative interviews and focus groups will establish the view of patients, their carers, healthcare personnel and commissioners towards current stroke and TIA care.

This work is part of the National Institute for Health Research, Collaborations for Leadership in Applied Health Research and Care (CLAHRC) programme. The main remit of this funding stream is to close the current gap between research and clinical practice.<sup>11-12</sup> As a result, a unique aspect of this project will be to combine research findings with routinely collected data in economic models and provide feedback to healthcare professionals and commissioners, working with them to develop strategies for change. This project will result in

more detailed information on stroke and TIA services than ever before along with specific plans for service development underpinned by reliable cost-effectiveness data. Evaluation will assess the gap between research and clinical practice and provide a model for future research into service improvement in the NHS.

## METHODS

### Study aims/research questions

The overriding aim of this study is to optimise the acute management of people with stroke and TIA in Birmingham through identification and breaking down of current barriers to timely and effective treatment. The project involves an iterative process beginning with observation of current practice. From this initial observation, the following research questions have been formulated:

1. How do stroke and TIA patients get to hospital and why do they choose these routes?
2. To what extent does prehospital and hyperacute hospital care impact the timeliness of subsequent treatment, especially thrombolysis?
3. Are risk factors for cardiovascular disease correctly measured and managed in Primary Care before and after stroke or TIA?
4. What impact would service redesign to increase the proportion of acute stroke patients receiving thrombolysis have on the cost-effectiveness of care and patient outcomes in terms of strokes averted and quality-adjusted life-years?
5. What are the queuing effects caused by intermittent TIA clinics and what impact would a move to clinic slots, 7 days a week, have on patient outcomes and cost-effectiveness?
6. What do patients (and their carers) see as positive or negative aspects of the acute stroke patient pathway?
7. How do patient perspectives differ from those of the healthcare personnel working in the stroke pathway?

These research questions will be answered using a mixed-methods approach, bringing together quantitative, qualitative and economic analyses. A major goal of the work is to integrate with the healthcare service in which the research is conducted, building lasting relationships that reduce the existing gaps between research and implementation.<sup>11-12</sup> Using this model will enable further research questions to be generated in conjunction with the healthcare providers, ensuring that they are timely and relevant.

### Study design

This is a longitudinal observational study of stroke and TIA management throughout the care pathway. The study will employ the Plan-Do-Study-Act cycles of implementation and evaluation.<sup>13</sup> This model is commonly used in quality improvement projects<sup>14-16</sup> and will be adapted for this project into three phases: assessment of current practice (recruitment of study participants and data collection), feedback (reporting of research

findings directly to service providers) and evaluation (of ongoing service change through further recruitment and data collection) (figure 1). Recruitment and collection of data relating to stroke and TIA services, respectively, will be staggered to ensure resources are used effectively.

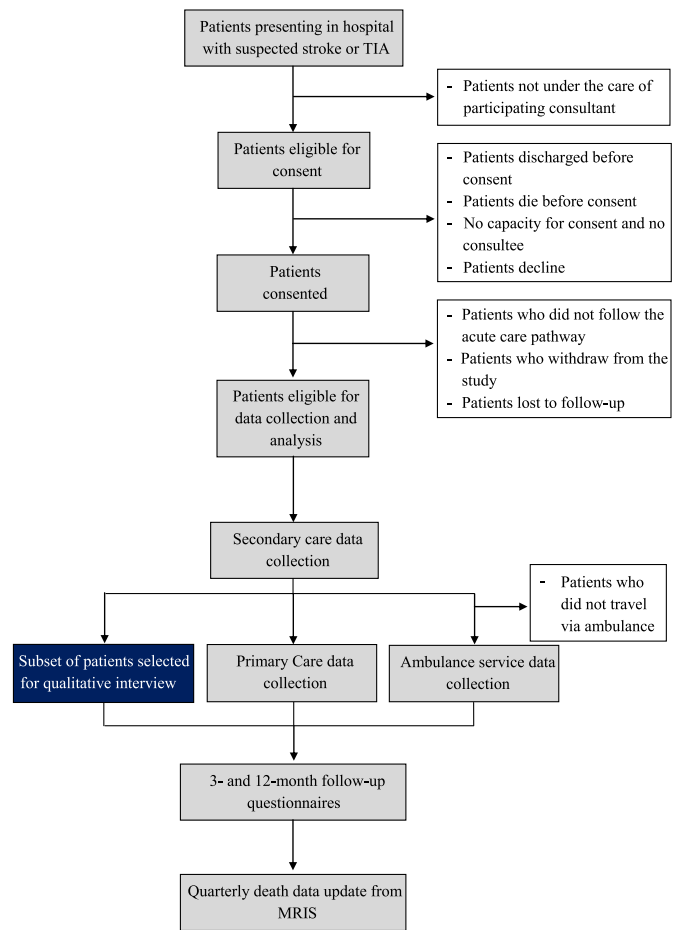
**Ethical considerations**

Although this study primarily involves service evaluation, ethical approval is required to allow collection of patient identifiers and sending out of quality-of-life questionnaires. Therefore, full ethical approval has been obtained from the National Research Ethics Service Committee, London—Queen Square (reference; 09/H0716/71) and site-specific R&D approval has been acquired from the relevant NHS trusts. In addition, participating trusts have given approval for anonymised data from clinical audits to be used within the quantitative analyses in this project.

**Study population/recruitment procedure**

The study will take place within two hospital trusts (University Hospitals Birmingham NHS Foundation Trust and Heart of England NHS Foundation Trust) and the surrounding Primary Care Trusts (South Birmingham, Birmingham East and North, Solihull, Sandwell, Dudley, Heart of Birmingham Teaching, Warwickshire, Worcestershire). Additional data relating to patients who travelled to hospital via ambulance will be collected from the West Midlands Ambulance Service NHS Trust (figure 2).

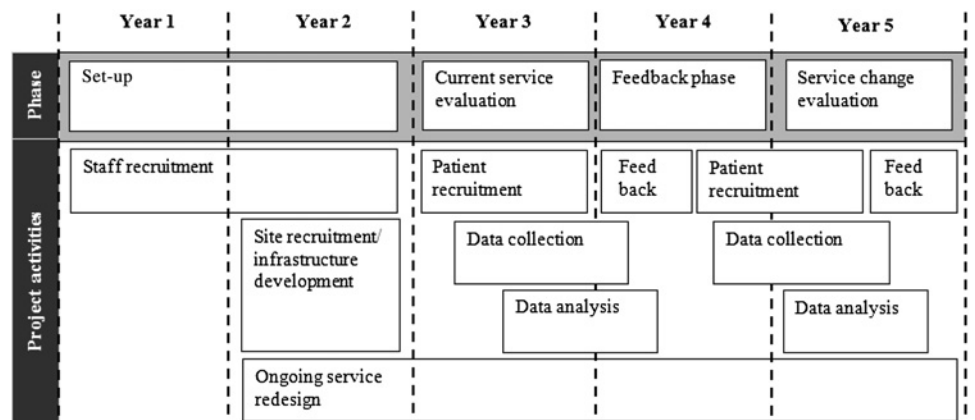
Patients will be recruited from stroke wards and TIA clinics in participating hospital trusts. Eligible patients will be those thought to be having a stroke or TIA who present to a collaborating hospital trust and are under the care of a participating stroke consultant during the data collection period (figure 2). Only patients unwilling or unable to give informed consent (and where no consultee is available) will be excluded. Informed consent will be gained from all patients to allow collection of patient identifiers and completion of quality-of-life questionnaires. Where an individual is unable to provide informed consent due to lack of capacity, assent from an appropriate consultee will be sought.



**Figure 2** Flow diagram of patient recruitment and data collection during the study. MRIS, Medical Research Information Service; TIA, transient ischaemic attack.

Patients eligible for the qualitative component of the project will be selected from those recruited to the main study. Purposive sampling will be used in recruitment to ensure that a range of patient experiences is captured. Patients will be given the option of having their carer, friend or family member attend the interview with them and they can refer to them in order to help fill in the gaps in their accounts. All parties attending interviews will provide written informed consent.

**Figure 1** Project timeline detailing phases and related activity throughout the project.



Healthcare personnel and commissioners will be interviewed, either on their own or in a focus group. Purposive sampling will be used to ensure recruitment of personnel across the care pathway, with study stakeholders acting as gatekeepers to recruit initial participants.

**Sample size**

No formal sample size calculation has been taken for this project. The nature of this study is that it is one of observation of current practice, and therefore, a sample size calculation was not deemed appropriate. However, based on validated data from both hospital trusts (2010–2011), approximately 400 patients with stroke and 350 patients with TIA attended each hospital each year. Based on our model of two 1-year data collection periods (the first being assessment of current practice and the second being an evaluation of practice change) (figure 1) and assuming around 75% recruitment of eligible patients, approximately 600 patients with stroke and 525 patients with TIA will be included per data collection period.

Within the qualitative component, interviews will be conducted with approximately 30 patients (some of whom will be accompanied by their carers). When 10 and 20 patients have been interviewed, a further theoretical sample will be sought,<sup>17</sup> guided by the emerging data analysis in order to extend and challenge earlier data and interpretation and to test the integrity and credibility of the developing analysis.<sup>18</sup> The proposed number of interviews will enable saturation of themes.<sup>19 20</sup> Healthcare professionals and commissioners will be selected in a similar vein, with up to 30 per stakeholder group.

**Data collection**

Data related to the patient’s present hospital admission/clinic appointment and preceding stroke/TIA event will be collected retrospectively from hospital medical records (table 1). Patient identifiers will be collected to allow identification of patient records in other participating NHS trusts.

General practitioner surgeries from the participating Primary Care Trusts will be invited to participate in the

**Table 1** Quantitative data collected from each healthcare setting

Healthcare setting	Time period*	Data collected	Examples
Primary Care	Pre- and post-stroke/TIA event	Measurement of cardiovascular risk factors	Blood pressure, cholesterol, smoking status, absolute cardiovascular risk score
		Management of cardiovascular risk factors Dates and times	Antihypertensive and statin prescriptions  Relating to GP consultations, cardiovascular risk factor measurements, prescriptions
Secondary Care	During stroke/TIA event	Patient identifiers	NHS number, patient name, date of birth and patient address
		Route to hospital  Inhospital investigations	Emergency ambulance, general practitioner referral, self referral to the emergency department  CT scan, blood pressure, cholesterol
		Treatment given Dates and times	Thrombolysis, carotid endarterectomy Relating to onset of symptoms, arrival in hospital, CT scan, first contact with medical/health professionals, admission to hospital, discharge from hospital, follow-up clinic appointment
Emergency Services	Pre-stroke/TIA event	Discharge medication	Antihypertensive and statin prescriptions
		Final diagnosis Presenting complaint Patient symptoms Emergency service investigations Medications administered Dates and times	Stroke, TIA, stroke mimic Suspected stroke, TIA, left-sided weakness Arm weakness, speech impediment, dizziness Face Arm Speech Test, blood pressure, heart rate, Glasgow Coma Score Saline solution (NaCl)  Relating to onset of symptoms, ambulance dispatch, arrival at patient, departure for hospital, arrival in the emergency department and handover of patient care
Medical Research Information Service	Post-stroke/TIA event	Date and time Cause of death	Of death As stated on death certificate

\*Time period (in relation to the patient’s stroke/TIA event) from which data were collected.  
GP, General Practitioner; TIA, transient ischaemic attack.



study, and data will be collected regarding Primary Care consultations, including primary and secondary prevention and outcome (table 1).

For those patients who travel to hospital via the Emergency Services, data will be extracted from the West Midlands Ambulance Service NHS Trust records. Relevant patient data will be identified using ambulance case and station numbers, extracted from hospital records. Data collected will include details of presenting complaints, patient symptoms, investigations conducted (eg, Face Arm Speech Test) and medications given (table 1). Timings from ambulance dispatch to arrival at hospital and handover will be acquired from the ambulance computer-aided dispatch system.

Additional anonymised data will be collected from all participating hospital trusts. These data will include demographics for all validated stroke admissions during each data collection period. This will be used to define the proportion of eligible patients successfully recruited to the study and whether these patients are representative of the general stroke population. Additional data regarding all scheduled TIA follow-up clinics will also be collected from both hospital sites for use in economic analyses.

Data from each NHS trust will be securely transferred into a bespoke web enabled SQL server database (Microsoft Corporation, Redmond, Washington, USA) stored securely at the host institution (University of Birmingham).

Qualitative data will be collected via in-depth interview or focus group. In-depth interviews will be used as they offer the most appropriate way to elicit people's beliefs and experiences.<sup>21 22</sup> Focus groups provide an opportunity for interaction between participants, allowing them to reflect on their own and others perspectives.<sup>23</sup> Flexibility in data collection is required to enable as broad a range of people to participate as possible, for example, focus groups are more appropriate in some of the healthcare environments.

Interviews and focus groups will follow a topic guide, developed iteratively as the study progresses.<sup>24</sup> Data will be collected from patients (and their carers) about their stroke and TIA experience and their treatment and care in relation to this. Healthcare personnel and commissioners will be asked about the stroke and TIA patient pathways, in particular, areas they think are good or that could be improved.

Following interviews and focus groups, the interviewer will write field notes,<sup>25</sup> noting the context and 'feel' of the interview (eg, if there were any points at which the participant was uncomfortable). Non-verbal communication will also be recorded in this. These field notes will be used in conjunction with interview transcripts during data analysis.

### Follow-up

Postal questionnaires will be sent to all recruited patients (who are still alive) at 3 and 12 months after the initial stroke/TIA event. These questionnaires will contain

health status assessments, including the Modified Rankin Score, EQ-5D and the Stroke Impact Scale. Patients' vital status will be checked using the NHS Personal Demographics Service, 1 week prior to sending the questionnaire.

Details of all recruited patients will be sent to the Medical Research Information Service at the NHS Information Centre (Leeds, England). They will provide quarterly follow-up data on all-cause mortality for all patients in the study (table 1).

## DATA ANALYSIS AND DISSEMINATION

### Epidemiological study

Quantitative data from all trusts will be collated and analysed to assess existing barriers to effective treatment for stroke and TIA. Previous literature assessing barriers to effective acute stroke care have focused primarily on public awareness<sup>26 27</sup> and hospital care.<sup>28–30</sup> The main focus of our analyses will be to use linked data from each patient to assess the impact of care across the clinical pathway (hence across clinical organisations), something that is not currently possible with routine clinical audits in the UK.<sup>8</sup> Descriptive statistics will be used to define current practice, and logistic regression analyses will evaluate associations between identified barriers to care and other influencing factors.

Epidemiological findings will be used to inform proposed strategies for change in the economic analyses of the stroke and TIA care pathway. In addition, trust-specific findings will be reported back to relevant parties through a series of tailored reports and presentations. This dissemination will offer a unique opportunity to feedback findings between trusts and facilitate joined-up service provision.

### Economic modelling study

In acute stroke, previous economic analyses have assessed the effects of thrombolysis against 'conservative treatment' (no thrombolysis).<sup>31–34</sup> In the present study, we intend to compare current care (including thrombolysis) with 'change strategies' designed to increase thrombolysis rates. Following the feedback phase of the project (figure 1), we will use the same modelling approach to examine whether ongoing service change has been effective.

Through work previously commissioned by the West Midlands Strategic Health Authority, a mathematical model has been developed that compares current practice with service redesign. This decision tree model maps out the acute stroke care pathway, using a series of probabilities (derived from epidemiological data collected), which predicts the likelihood a patient will access a specific service or be given a type of treatment. The model will be used to evaluate the impact of treatment decisions on NHS costs and patient outcomes (death and quality of life). These costs will be derived from a combination of standard unit costs, NHS reference costs and previously published literature.<sup>31 35</sup>

Health status data will be collected directly from patients using 3- and 12-month follow-up questionnaires and supplemented with published data.<sup>31</sup>

Our group has also previously developed a mathematical model, which aims to determine the optimum pattern of service provision for people presenting with a TIA or minor stroke.<sup>36</sup> This discrete event simulation model examines the workload and cost implications of various methods of organising care. In the present study, the model will be used to track individuals who are occasionally competing for resources in a realistic representation of calendar time (the availability of these resources depends on time of day and day of week). This will allow estimation of the impact of redesigning TIA services on NHS costs and patient outcomes. Once again, the model will be based on real-life data collected from recruited patients and anonymised data from the hospital trusts.

Economic modelling is relevant in this situation as it allows comparison of different patterns of service provision in a systematic fashion where trial comparison would be impracticable. The findings of these studies will be fed back to participating trusts through reports and presentations. Specifically, service commissioners will be engaged, and these data will be central to future commissioning of stroke services across the participating Trusts.

### Qualitative study

Qualitative methodologies offer the most appropriate way to elicit people's beliefs, knowledge and the meanings they ascribe to their experiences.<sup>21 22</sup> In this study, these methodologies will be used to examine what barriers to service delivery, implementation and use, patients and healthcare professionals experience along the stroke and TIA care pathway.

Interview transcripts will be read and checked for accuracy and then entered into a computerised database using the NVivo software package (QSR International Pty Ltd, Doncaster, Victoria, Australia). Data analysis will be conducted using constant comparative analysis, with examination of deviant cases.<sup>37 38</sup> Coding processes, including creating OSOPs,<sup>24</sup> will identify emerging key categories and concepts from the participant data. These will be compared across interviews and time of data collection in order to capture the process of change. Concepts identified will further be compared against established concepts in the literature and will be integrated into themes providing a structure for presentation of findings. Researchers from a number of disciplines (sociology, public health, nursing and primary care) will be involved in the analysis, allowing for a range of insights to be gained.<sup>24</sup> Other steps to ensure rigour will include: having two (or more) researchers independently code initial transcripts and then compare findings to formulate an initial coding frame.

Findings will be fed back to participating trusts in conjunction with epidemiological and economic

modelling feedback. This qualitative element of the project will offer a unique insight to the overall study findings and facilitate service redesign, which is better tailored to patient and practitioner needs.

### CONCLUSIONS

The CLAHRC Optimisation of the Management of Stroke and TIA project will build on previous work by describing current practice in stroke and TIA care<sup>8 9</sup> and examine the potential effects of implementation of the National Stroke Strategy.<sup>7</sup> By working together with multiple healthcare trusts, this study aims to improve patient care right across the stroke and TIA care pathway. Using a generalisable model, data collection, analysis, feedback and evaluation will be carried out within the life of this project. This model of research, feedback and evaluation will be assessed for its potential to set the foundations for how healthcare services are routinely examined and optimised in the future.

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**Competing interests** None.

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### REFERENCES

1. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurol* 2007;6:182–7.
2. Wardlaw JM, Murray V, Berge E, *et al*. Thrombolysis for acute ischaemic stroke. *Cochrane Database Syst Rev* 2009;(4):CD000213.
3. Chung H, Refoios CR, Barnett D. Alteplase for the treatment of acute ischaemic stroke: NICE technology appraisal guidance. *Heart* 2007;93:1616–17.

4. Wahlgren N, Ahmed N, Davalos A, *et al.* Thrombolysis with alteplase 3-4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. *Lancet* 2008;372:1303–9.
5. Rothwell PM, Giles MF, Flossmann E, *et al.* A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. *Lancet* 2005;366:29–36.
6. National Institute for Health and Clinical Excellence (NICE). *Diagnosis and Initial Management of Acute Stroke and Transient Ischemic Attack (TIA)*. NICE CG068. NICE Clinical Guideline. London: NICE, 2008.
7. Department of Health. *National Stroke Strategy*. London: Crown, 2007.
8. Henssge U, Hoffman A, Kavanagh S, *et al.* *The National Sentinal Stroke Audit 2010. Round 7*. London: Royal College of Physicians, 2011:1–74.
9. The Intercollegiate Stroke Working Party. *National Sentinal Stroke Audit—Organisation of Care 2010. Round 7*. London: Royal College of Physicians, 2010.
10. McElduff P, Lyratzopoulos G, Edwards R, *et al.* Will changes in primary care improve health outcomes? Modelling the impact of financial incentives introduced to improve quality of care in the UK. *Qual Saf Health Care* 2004;13:191–7.
11. Black N. The Cooksey review of UK health research funding. *BMJ* 2006;333:1231–2.
12. Cooksey D. *A Review of UK Health Research Funding*. London: The Stationery Office, 2006.
13. Langley GJ, Nolan KM, Nolan TW, *et al.* *The Improvement Guide. A Practical Approach to Enhancing Organizational Performance*. San Francisco, CA: Jossey-Bass, 1996.
14. Fortney J, Enderle M, McDougall S, *et al.* Implementation outcomes of evidence-based quality improvement for depression in VA community based outpatient clinics. *Implement Sci* 2012;7:30.
15. Koetsier A, van der Veer SN, Jager KJ, *et al.* Control charts in healthcare quality improvement. A systematic review on adherence to methodological criteria. *Methods Inf Med* 2012;51:189–98.
16. White CM, Statile AM, Conway PH, *et al.* Utilizing improvement science methods to improve physician compliance with proper hand hygiene. *Pediatrics* 2012;129:e1042–50.
17. Glaser B, Strauss AL. *The Discovery of Grounded Theory: Strategies for Qualitative Research*. Chicago: Aldine, 1967.
18. Strauss AL, Corbin J. *Basics of Qualitative Research, Grounded Theory Procedures*. London: Sage, 1990.
19. Morse JM. Determining sample size. *Qual Health Res* 2000;10:3–5.
20. DePaulo P. Sample size for qualitative research. The risk of missing something important. *Quirk's Marketing Research Review*. 2000: Article No.636.
21. Denzin N, Lincoln Y. *Entering the Field of Qualitative Research*. Thousand Oaks: Sage, 1994.
22. Britten N. Qualitative interviews in medical research. *BMJ* 1995;311:251–3.
23. Finch H, Lewis J. Focus groups. In: Ritchie J, Lewis J, eds. *Qualitative Research Practice: A Guide for Social Science Students and Researchers*. London: Sage, 2003:170–98.
24. Ziebland S, McPherson A. Making sense of qualitative data analysis: an introduction with illustrations from DIPEX (personal experiences of health and illness). *Med Educ* 2006;40:405–14.
25. Corbin J, Strauss A. Memos and diagrams. In: Corbin J, Strauss A, eds. *Basics of Qualitative Research 3e*. London: Sage, 2008: 117–41.
26. Hodgson C, Lindsay P, Rubini F. Can mass media influence emergency department visits for stroke? *Stroke* 2007;38:2115–22.
27. Yoon SS, Heller RF, Levi C, *et al.* Knowledge of stroke risk factors, warning symptoms, and treatment among an Australian urban population. *Stroke* 2001;32:1926–30.
28. Harraf F, Sharma AK, Brown MM, *et al.* A multicentre observational study of presentation and early assessment of acute stroke. *BMJ* 2002;325:17.
29. Kwan J, Hand P, Sandercock P. A systematic review of barriers to delivery of thrombolysis for acute stroke. *Age Ageing* 2004;33:116–21.
30. Lindsberg PJ, Hoppola O, Kallela M, *et al.* Door to thrombolysis: ER reorganization and reduced delays to acute stroke treatment. *Neurology* 2006;67:334–6.
31. Sandercock P, Berge E, Dennis M, *et al.* Cost-effectiveness of thrombolysis with recombinant tissue plasminogen activator for acute ischemic stroke assessed by a model based on UK NHS costs. *Stroke* 2004;35:1490–7.
32. Mar J, Begiristain JM, Arrazola A. Cost-effectiveness analysis of thrombolytic treatment for stroke. *Cerebrovasc Dis* 2005;20:193–200.
33. Ehlers L, Andersen G, Clausen LB, *et al.* Cost-effectiveness of intravenous thrombolysis with alteplase within a 3-hour window after acute ischemic stroke. *Stroke* 2007;38:85–9.
34. Araujo DV, Teich V, Passos RB, *et al.* Analysis of the cost-effectiveness of thrombolysis with alteplase in stroke. *Arq Bras Cardiol* 2010;95:12–20.
35. Ward S, Lloyd JM, Pandor A, *et al.* A systematic review and economic evaluation of statins for the prevention of coronary events. *Health Technol Assess* 2007;11:1–160, iii-iv.
36. Mant J, Barton PM, Ryan RP, *et al.* *What Is the Optimum Model of Service Delivery for Transient Ischaemic Attack?* London: Report for the National Co-ordinating Centre for NHS Service Delivery and Organisation (NCCSDO), 2007.
37. Glaser BG, Strauss AL. *The Constant Comparative Method of Qualitative Analysis. The Discovery of Grounded Theory: Strategies for Qualitative Research*. New York: Aldine de Gruyter, 1999.
38. Green J, Britten N. Qualitative research and evidence based medicine. *BMJ* 1998;316:1230–2.