Identifying Optimal Pathways of Care in the Delivery of Carotid Interventions

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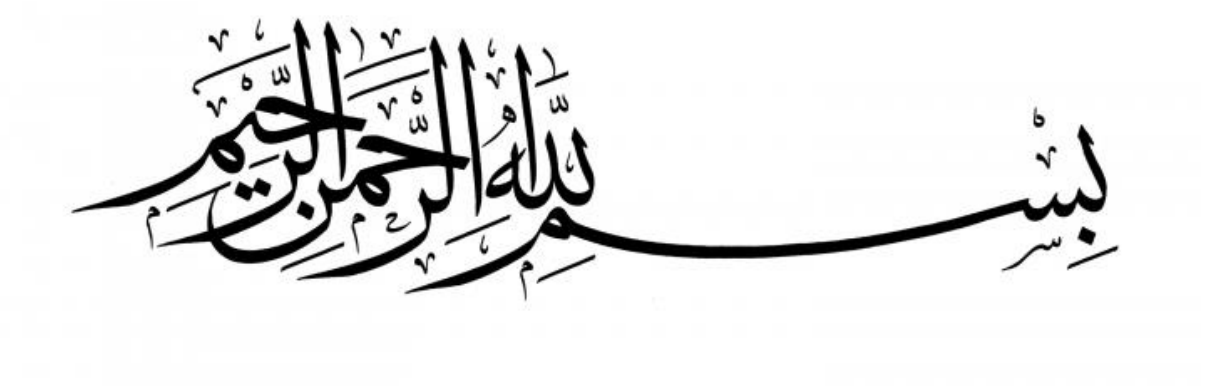

“In the name of Allah (God), the Most Gracious, the Most Merciful and Compassionate”



“Oh my Lord! Increase me in knowledge”

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Declaration of Originality

I confirm that the work conducted in this thesis has been undertaken by myself, under the supervision of Mr Richard Bulbulia, Mr Prem Chana, Professor Alison Halliday and Professor Martin Landray. I declare no conflicts of interest.

This research project was completed despite disruption caused by the coronavirus pandemic.

Chapter 1: I composed the chapter. Some sections are based on 2 papers and a book chapter I co-authored. These have been referenced.

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Chapter 8: I composed the chapter based on a paper I co-authored. This has been referenced.

This thesis is my own work and has not been submitted for a degree at any other University.



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Abbreviations

AAA	Abdominal Aortic Aneurysm
ACAS	Asymptomatic Carotid Atherosclerosis Trial
ACST	Asymptomatic Carotid Surgery Trial
ACT	Asymptomatic Carotid Trial
AI	Artificial Intelligence
ANP	Advanced Nurse Practitioner
BEFAST	Balance, Eye symptoms, Face, Arm, Speech, Time to call 999
CAS	Carotid Artery Stenting
CAVATAS	Carotid and Vertebral Artery Transluminal Angioplasty Study
CEA	Carotid Endarterectomy
CHF	Congestive Heart Failure
CI	Confidence Interval
CMS	Centers for Medicare and Medicaid Services
CMT	Contemporary Medical Therapy
CQC	Care Quality Commission
CREST-1	Carotid Revascularisation Endarterectomy versus Stenting Trial
CREST-2	Carotid Revascularisation and Medical Management for Asymptomatic Carotid Stenosis Trial
CRF	Chronic Renal Failure
CSTC	Carotid Stenting Trialists' Collaboration
CT	Computerised Tomography
DALY	Disability-Adjusted Life Year
DM	Diabetes Mellitus
EBM	Evidence-Based Medicine
ECST	European Carotid Surgery Trial
ED	Emergency Department
EMBASE	Excerpta Medica Database
EPD	Embolic Protection Device

ESC	European Society of Cardiology
ESVS	European Society for Vascular Surgery
EU	European Union
EVA-3S	Endarterectomy Versus Angioplasty in patients with Symptomatic Severe Carotid Stenosis
FAST	Face, Arm, Speech, Time to call 999
FCE	Finished Consultant Episode
FMEA	Failure Mode and Effect Analysis
GA	General Anaesthesia
GALA	General Anaesthesia versus Local Anaesthesia for Carotid Surgery
GC	Global Comparators'
GDP	Gross Domestic Product
GIRFT	Get It Right First Time
GP	General Practitioner
HASU	Hyper-Acute Stroke Unit
HDU	High Dependency Unit
HES	Hospital Episode Statistics
HESID	Hospital Episode Statistics Identification
HFMEA	Healthcare Failure Mode and Effect Analysis
HR	Hazard Ratio
HRO	High Reliability Organisation
HTN	Hypertension
ICD	International Classification of Diseases
ICSS	International Carotid Stenting Study
ICU	Intensive Care Unit
IHD	Ischaemic Heart Disease
IMD	Index of Multiple Deprivation
LA	Local Anaesthesia
LDL-C	Low Density Lipoprotein Cholesterol

LOS	Length of Stay
MDT	Multi-Disciplinary Team
MEDLINE	Medical Literature Analysis and Retrieval System Online
MI	Myocardial Infarction
MRI	Magnetic Resonance Imaging
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NBM	Nil By Mouth
NHS	National Health Service
NIS	Nationwide Inpatient Sample
NNT	Number Needed to Treat
NVR	National Vascular Registry
OECD	Organisation for Economic Cooperation and Development
OMT	Optimal Medical Therapy
ONS	Office for National Statistics
OPCS	Office of Population Censuses and Surveys Classification of Interventions and Procedures
OR	Odds Ratio
PCSK-9	Proprotein Convertase Subtilisin/Kexin type 9
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PVD	Peripheral Vascular Disease
QIP	Quality Improvement Project
RCT	Randomised Clinical Trial
RESGOR	Government Office Region of Residence
RR	Relative Risk
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy
SEIPS	Systems Engineering Initiative for Patient Safety
SICU	Surgical Intensive Care Unit
SPACE-1	Stent-Protected Angioplasty versus Carotid Endarterectomy

SPACE-2	Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis versus Carotid Endarterectomy
TCAR	Trans-Carotid Arterial Revascularisation
TIA	Transient Ischaemic Attack
UK	United Kingdom
USA	United States of America
USD	United States Dollar
VACS	Veteran Affairs Cooperative Study
VSGBI	Vascular Society of Great Britain and Ireland
WHO	World Health Organisation

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Thesis Abstract

Background: Successful carotid endarterectomy (CEA) and carotid artery stenting (CAS) halve long-term stroke risk but are potentially hazardous. Optimising the carotid intervention pathway may reduce harm.

Aims: This thesis used qualitative and quantitative methodologies to identify: hospital-level factors affecting CEA and CAS procedural outcomes; failures in the CEA pathway for improvement; temporal and regional trends in CEA and CAS provision and outcomes; and patient-level factors affecting procedural and long-term outcomes.

Qualitative Methods and Results: A systematic review of 124,958 patients showed that large hospitals, serving large populations, with vascular beds, clinical pathways and Vascular Surgeons performing CEA were associated with improved outcomes. An ethnographic study, involving 1,072 hours of observations of the CEA pathway in symptomatic patients, identified 110 patient safety incidents primarily in documentation, public health awareness and the care-providing environment. A Healthcare Failure Mode and Effect Analysis of 65 organisational failures by 13 stakeholders recommended patient education to improve stroke recognition, increasing resources, implementing technology, standardising care and improving communication to optimise the CEA pathway.

Quantitative Methods and Results: A 16-year analysis of 68,897 English patients in the Hospital Episode Statistics dataset showed that CEA and CAS age-standardised rates reduced since 2011-2012 with regional variation in provision. Despite temporal improvements in most CEA procedural outcomes, regional variation existed in CEA and CAS outcomes. Prior stroke and congestive heart failure were associated with adverse CEA and CAS procedural outcomes whilst ischaemic heart disease, peripheral vascular disease, diabetes mellitus, chronic renal failure, age 70 years and above and non-White ethnicity were associated with increased CEA risk. Increased deprivation was associated with CEA mortality but did not affect CAS outcomes. Similar risk factors existed for long-term stroke risk following CEA and CAS.

Conclusions: Organisational and patient-level factors have been identified for optimising the carotid intervention pathway. Implementing these findings may reduce harm in high-risk patients undergoing carotid interventions, maximising their effectiveness.

CHAPTER 1: Introduction

Annually, 43,000 vascular procedures are performed in England by 450 Consultant Vascular Surgeons across 70 National Health Service (NHS) Trusts.[1] This includes carotid endarterectomy (CEA) and carotid artery stenting (CAS) to reduce long-term stroke risk.

This thesis' focus will be identifying factors that contribute to adverse CEA and CAS outcomes by causing harm along the patient pathway. These factors could then be optimised to reduce the risk of procedural complications.

This introductory chapter will introduce the specialty of Vascular Surgery, the role of Vascular Surgeons and the structure of vascular services in the United Kingdom (UK). The effect of healthcare structure on quality of care will then be discussed. Randomised clinical trial (RCT) evidence for performing CEA and CAS in symptomatic and asymptomatic patients will be presented before future developments are considered.

What is Vascular Surgery?

Vascular Surgeons treat disorders of arteries, veins and lymphatics. Most cases relate to arterial pathology caused by systemic atherosclerosis. Vascular Surgeons operate throughout the body (except intracranially and on coronary vessels) to improve perfusion of organs and limbs if contemporary medical therapy (CMT) fails to treat the condition. Due to the generalised nature of vascular disease, patients usually suffer from pathology in numerous vascular beds. This may manifest as a history of myocardial infarction (MI), stroke and/or renal impairment. Moreover, due to the association between smoking and atherosclerosis, most vascular patients are either current or past smokers, which may result in respiratory impairment. They may also suffer from diabetes mellitus (DM), hypertension (HTN), hypercholesterolaemia, ischaemic

heart disease (IHD), congestive heart failure (CHF), peripheral vascular disease (PVD) and/or chronic renal failure (CRF) and are high-risk for procedural complications.

Therefore, endovascular procedures are increasingly being adopted, especially in patients unfit for open surgery. However, concerns remain regarding their long-term durability, need for re-intervention and cost, requiring ongoing research.

Role of Vascular Surgeons

The Royal College of Surgeons of England[2] and the Vascular Society of Great Britain and Ireland (VSGBI)[3] list the following core activities of Vascular Surgeons:

- Prevent death from abdominal aortic aneurysms (AAAs) and strokes
- Heal leg ulceration from arterial, venous or diabetic pathologies
- Prevent limb amputation
- Promote cardiovascular health
- Improve quality of life of vascular patients
- Assist colleagues in managing vascular complications of DM and CRF
- Provide renal access for CRF patients requiring haemodialysis

These activities are performed with 50% of patients presenting to vascular services acutely, requiring urgent or emergency intervention.[2, 3]

The average patient's age is also increasing, with worsening comorbidities. This requires a rigorous assessment and management of risk factors to optimise outcomes. This is through

consultation with Medical specialties and other members of the multi-disciplinary team (MDT), such as Vascular Scientists, Rehabilitation Specialists, Prosthetics, Podiatry, Occupational Therapists, Physiotherapists, Pharmacists and Dieticians. Increased emphasis on endovascular treatments also requires collaboration with Interventional Radiologists.

Vascular Surgeons are also required to publish their outcomes. This clinical governance activity is mandatory for revalidation and commissioning of vascular services.[3] Consultant Vascular Surgeons input vascular and endovascular procedures and outcomes into the National Vascular Registry (NVR), for audit and research, allowing monitoring of outcomes and evaluating new therapies.

Vascular units have high bed occupancy rates, endovascular equipment is expensive and surgical procedures are technically demanding, time-consuming and patients may require Critical Care admission post-operatively. Re-admission rates are also substantial due to disease progression. Therefore, vascular services need to be structured to maximise efficiency.

Vascular Services in the UK

The VSGBI proposed centralisation of vascular services in its *Provision of Services for Patients with Vascular Disease* document[3] which recommended restructuring into 'hub and spoke' networks. These would consist of an 'arterial hospital' (the 'hub') providing arterial surgery, complex endovascular procedures and receiving acute referrals whilst day-case procedures and clinics would be provided at 'non-arterial hospitals' ('spokes').[3]

The VSGBI[3] suggested the following characteristics of the arterial hub:

- 24-hour Consultant Vascular Surgeon and/or Interventional Radiologist on-call
- Minimum of 6 Consultant Vascular Surgeons per unit
- 24-hour Emergency Vascular Operating Theatre
- 24-hour access to imaging
- 24-hour Critical Care with Anaesthetist, mechanical ventilation and renal support
- Vascular wards (with minimum 20-25 beds)
- At least one endovascular theatre or hybrid suite, with high-quality imaging
- At least 60 AAA and 40 CEA procedures per annum, averaged over three years
- Minimum population of 800,000 served
- On-site vascular laboratory
- At least weekly MDT meetings

Non-arterial spokes allow local assessment and diagnosis of vascular disease and provision of day-case procedures. Consultant Vascular Surgeons visit 3-5 days per week from the arterial hub to undertake clinics and review patients referred to Vascular Surgery (ideally within 48 hours).[3] Repatriation from hubs to spokes for rehabilitation also frees beds in the arterial centre for urgent and emergency admissions.

This structure allows Vascular Surgery to be delivered locally to patients, without needing to travel long distances unless complex arterial intervention is required. It also allows resources to be concentrated in fewer centres. It is important to understand the structure of a healthcare service as it can affect the quality of care and subsequent outcomes.

Healthcare Structure and Quality of Care

Avedis Donabedian[4] described three factors that influence the quality of care that patients receive. 'Structural factors' assess the systemic/organisational elements that reflect the setting in which care is delivered and their impact on quality of care.[4] This may include resource availability (e.g. access to Critical Care beds). 'Process factors' assess the quality of care that a patient receives.[4] For example, Hannan *et al*.[5] demonstrated that use of shunts, patches, eversion and protamine reduced CEA complications. 'Outcome measures' are best established in the surgical literature and assess the quality of the results of interventions.[4] This includes mortality rates, complication rates, length of stay (LOS) in hospital or re-admission rates.

Structural factors can be assessed swiftly and inexpensively. However, data are usually retrospective and administrative[6] which may not be accurately recorded. There is also a risk of confounding.[6] Significant reorganisation is required to implement structural changes whilst isolating the biggest contributor to increased quality of care can be difficult.[6] Process factors are usually evidence-based interventions that are easily assessed and altered.[6] However, evidence-based interventions are not suitable for all patients so adjusting for this variation is problematic.[6] Large amounts of data may also be required to identify process failures. This is laborious and may not accurately assess surgical complications due to technical failure (e.g. the cause of anastomotic leak).[6] Outcome measures have been adopted enthusiastically as they are seen to be the most accurate in assessing the quality of care that a patient receives and can identify areas for improvement.[6] However, due to complication rates of most procedures being low, large amounts of data may be required for sufficient power to determine benefit from different interventions.[6] The process of collecting outcomes may also improve them. This so-called 'Hawthorne effect'[6] confounds outcomes-based research. Table 1.1 summarises examples, advantages and disadvantages of structural, process and outcome factors.

Table 1.1: Examples, advantages and disadvantages of the various components of the Donabedian model of healthcare structure.

	Structural Factors	Process Factors	Outcome Factors
Examples	• Number of hospital beds • Size of population served • Number of intensive care beds	• Patch closure of arteriotomy • Use of intra-operative heparin • Dual anti-platelet agents	• Mortality rate • Complication rate • Re-admission rate
Advantages	• Readily measurable • Can have a large effect	• Easily assessed • Change can be made easily	• Adopted enthusiastically • Directly assess the result of the intervention
Disadvantages	• Reorganisation required to institute changes • Isolating biggest contributor problematic (confounding)	• Evidence-based interventions may not be suitable for all patients • Large amount of data required to identify failures	• Large amount of data required to identify failures • Hawthorne effect – collecting outcomes improves them

Therefore, quality of healthcare delivery should be assessed using a combination of all factors as they evaluate different aspects of patient care. A systematic review[7] of patients receiving vascular interventions reported that more than half of studies (31/57) evaluated outcome measures, one third (19/57) assessed structural factors and 7/57 studies examined process factors.[7] Therefore, there should be increased emphasis on assessing structural and process factors, whilst measuring outcomes, to improve the quality of care of vascular patients.

In the United States of America (USA), the Institute of Medicine's Committee on Quality of Health Care's document *To Err Is Human: Building a Safer Health System*[8] suggested implementing safety systems to safeguard against harm occurring due to structural factors. The National Center for Patient Safety was created to foster a system-orientated approach to patient safety that encourages adverse event reporting for learning and improvement.[9]

Crossing the Quality Chasm: A New Health System for the 21st Century[10] was subsequently published, aiming to improve six aspects of healthcare delivery, including the system being:

- safe to patients
- effective
- patient-centred
- timely
- efficient
- equitable

These factors should be considered when assessing the quality of care that patients receive. However, the system in which care is delivered can also contribute to harm.

Iatrogenic Harm

Iatrogenic harm is common in healthcare and causes morbidity and mortality. The scale of medical error and harm presents an opportunity to improve the quality of patient care whilst reducing healthcare expenditures and litigation costs.

The Harvard Medical Practice Study[11, 12] first reported adverse events occurring in 3.7% of 30,121 patients, with substandard care contributing to 27.6% of adverse events[11] whilst 47.7% were associated with surgery.[12] Disability lasted less than 6 months in 70.5% of adverse events, permanent disability occurred in 2.6% and 13.6% were fatal.[11] Another American study reported an adverse event rate of 2.9% in 15,000 patients.[13] Substandard care contributed to 30.0% of events whilst surgery was associated with 44.9%.[13] Permanent disability occurred in 16.6% and death in 6.6%.[13] Gawande *et al*.[14] reported 54.0% of adverse surgical events were preventable, particularly during lower limb bypass operations and AAA repairs.

In the UK, Vincent *et al*.[15] reported an adverse event rate of 10.8% in 1,014 patients. When multiple adverse events occurring in the same patient were included, this increased to 11.7%.[15] Minimal impairment by 1 month occurred in 66.0%, permanent impairment in 6.0% and 8.0% died.[15] This cost the NHS £290,268 but 48.0% of adverse events were preventable.[15] In another UK study, 8.7% of 1,006 admissions suffered an adverse event, resulting in disability lasting longer than 6 months in 15.0% and death in 10.0%.[16] Of these, 31.0% were preventable.[16]

Internationally, the adverse event rate ranged between 5.7-21.9% in studies conducted in Australia, Denmark, New Zealand, Canada, Holland and Sweden with 36.9-70.0% of adverse events deemed preventable, especially in surgical patients.[17-23] Rates of iatrogenic harm are comparable between countries with diverse healthcare systems. The large proportion of preventable adverse events, particularly related to surgery, allows an opportunity to improve patient care if our understanding of human error allows safeguards to be implemented.

A 'System Approach' to Error

James Reason[24] argued shifting the emphasis from a 'person approach' to a 'system approach' to understand errors in healthcare. Historically, blame was apportioned to an individual if harm occurred to a patient ('person approach'). This was explained by characteristics of human fallibility such as inattention, carelessness or negligence[24] and may have resulted in disciplinary measures and so-called 'naming and shaming'. This was demonstrated in the General Medical Council versus Dr Bawa-Garba (2018) case[25] where a Paediatric Registrar was removed from the UK medical register and convicted of manslaughter after the death of a 6-year-old boy. However, there were multiple systemic factors that contributed to the child's death, including staff shortages, lack of Consultant availability, failure of the laboratory test system and deficiencies in handover.[25] Dr Bawa-Garba was subsequently reinstated to the medical register in August 2018 after the Court of Appeal overturned the High Court's original decision.

An alternative perspective for understanding human error would be to use the 'system approach'. This recognises that errors occur due to systemic/organisational factors that require the incorporation of safeguards against these system failures.[24] When harm occurs, the emphasis is not on individuals but processes, encouraging learning from adverse event reporting. This philosophy is evident in the aviation industry, where 90% of incidents are reported without blame, fostering a culture of openness without fear of reprisals.[26]

The 'Swiss Cheese Model'

When an adverse event is caused by a system failure, this is usually due to failures of multiple safeguards, including technological, procedural and administrative factors. These modalities also have weaknesses which have been likened to holes in slices of Swiss cheese.

The ‘holes’ arise from ‘active failures’ or ‘latent conditions’.[24] Active failures are “unsafe acts committed by people in contact with the patient or system”.[24] These might include mistakes or violations of established protocols[24] and form the basis for blame in the person approach. Latent conditions are factors that exist within an organisation that predispose to a system failure.[24] They include time pressure, understaffing, inadequate equipment and unworkable protocols.[24] These latent conditions undermine safeguards in the system.

In isolation, these weaknesses do not compromise safety. However, when holes in multiple layers of the safeguarding strategy line up, even if momentarily, this can allow potential hazards to cause harm. Recognising that latent conditions can be altered before an adverse event occurs is integral to risk management using a system approach and forms the basis of recommendations by the Joint Commission[27] (in the USA) and the Francis Report[28] (in the UK) to risk assess healthcare processes. This strategy has been implemented in other industries.

High Reliability Organisations (HROs)

Industries that operate in high-risk environments successfully are termed HROs. USA Navy nuclear aircraft carriers, nuclear power plants and air traffic control centres were the original HROs studied.[29, 30] Workers within these HROs perform complex tasks and demanding activities, individually and in teams, under time pressure, with good outcomes, despite handling equipment that could cause devastating consequences if a major failure occurred.

Similarities between HROs and the delivery of healthcare allow insights to be gained into improving surgical outcomes. HROs function effectively because they demonstrate resilience. During routine functioning, a hierarchical structure exists. However, during emergencies, responsibility is devolved to the most appropriate person with the expertise to successfully

manage the situation. This is similar to the Operating Theatre where a Consultant often supervises a Trainee performing surgery. However, if a problem arises, the Consultant takes control and manages the issue before allowing the Trainee to continue in a controlled environment. This flexibility in approach allows crises to be managed effectively.

HROs also maintain situational awareness. This is similar to the operating Surgeon who, despite being engrossed, maintains situational awareness to ensure the team is functioning effectively. Healthcare delivery is reliant on protocols to manage patients in a reproducible way. This contrasts with HROs which encourage variability of human action in adapting to changing circumstances as a safeguard against adverse events.

Another feature of HROs is their focus on the potential for failure. Errors are expected and workers are trained to recognise errors and mitigate against them. Systemic reforms are preferred to specific changes and novel errors are constantly considered. This preoccupation with error does not exist in healthcare but may be a valuable approach to minimising harm, especially given its complexity and the potential to blame individuals at the end of healthcare processes when errors occur.

The Carotid Intervention pathway

Carotid interventions halve long-term stroke risk. However, the risk of harm occurring is high because the decision-making process is complex. Carotid intervention pathways are becoming increasingly complex and patients more co-morbid in a healthcare system under pressure.

A typical journey involves an individual experiencing a stroke or transient ischaemic attack (TIA) and being reviewed in the community or Emergency Department (ED). Following

referral for a consultation by a Stroke Physician or Neurologist (as an inpatient or outpatient), they may then require specialist investigations before being reviewed by a Vascular Surgeon.

This complex pathway commences at unpredictable times and requires coordination of various specialties in multiple locations. There is also time pressure as recurrent stroke risk is high. UK guidelines[31, 32] recommend that the delay between symptoms and CEA should be less than two weeks. The *Get It Right First Time (GIRFT) Programme National Specialty Report* for Vascular Surgery[1] (a Clinician-led NHS improvement programme aiming to share best practice and improve outcomes) suggested reducing time from symptoms to CEA to 7 days.

This thesis will examine systemic factors along the patient pathway that affect CEA and CAS outcomes. However, the evidence base for carotid interventions will be discussed first.

The Burden of Stroke

In the UK, more than 100,000 people have a stroke annually and 12.5% die within 30 days.[33] Strokes are the fourth largest cause of death and a substantial cause of disability, with almost 1 million British adults affected.[33] The estimated cost of stroke to the UK economy is £26 billion per annum, with care costs accounting for £15.8 billion and new cases of stroke costing £5.3 billion.[34] The Global Burden of Disease study[35] reported that stroke was the third commonest cause of globally lost disability-adjusted life years (DALYs) in 2017. Since 2007, the mean percentage increase in lost DALYs globally has been 17.4% in males and 13.6% in females.[35] Globally, stroke is the third commonest cause of death, with atherosclerotic carotid artery stenosis implicated in 20-25% of all strokes.[36] Even asymptomatic carotid artery stenosis confers more than 3% increased stroke risk in the following year (a greater than 50% increased relative risk (RR)).[37] CEA and CAS are effective stroke prevention strategies.

CEA: The Technique

CEA can be performed under local anaesthesia (LA) or general anaesthesia (GA), with or without a shunt. The General Anaesthesia versus Local Anaesthesia for Carotid Surgery (GALA) trial reported no difference in stroke or mortality rates between the two types of anaesthesia in patients undergoing CEA.[38] The operation begins with an oblique incision, following the anterior border of sternocleidomastoid.[39] This is retracted and the bifurcation dissected out. Heparin is administered intravenously and internal, external and common carotid arteries clamped.[39] A longitudinal arteriotomy is extended from the common carotid artery into the internal carotid artery.[39] The plaque is removed and the artery repaired with primary closure or patch placement (conventional CEA).[39] Similar peri-operative major stroke and death rates have been described between eversion and conventional CEA in the Eversion Carotid Endarterectomy versus Standard Trial.[40] The incidence of early carotid artery occlusion and re-stenosis at mean follow-up of 14.9 months was also similar between the 2 groups.[40]

Performing CEA also has risks: stroke; cranial nerve injury; MI; and haematoma.[41] Patients with concurrent coronary artery disease and contralateral carotid artery occlusion are considered high-risk for CEA.[42, 43] Other factors that make CEA more technically difficult include a high bifurcation, recurrent stenosis, contralateral cranial nerve palsies, previous radical neck dissection and radiation.[41] In these patients, CAS may be an alternative.[44-46]

CAS: The Technique

CAS can be performed under LA or GA. A catheter is inserted percutaneously (usually into the common femoral artery) and advanced until the common carotid artery is reached.[39] A guidewire is deployed across the stenosis so a stent can be placed and a balloon inflated to

expand the stent.[39] Embolic protection devices (EPDs) can minimise embolisation of atherosclerotic material distal to the stenosis, reducing the risk of neurological ischaemia.[39]

CAS is less invasive than CEA and may be performed in high-risk patients with comorbidities whilst potentially treating lesions inaccessible by surgery. However, studies have shown that CAS may carry a higher procedural stroke risk than CEA in symptomatic patients.[47, 48]

Registry data (and post-hoc analyses of RCTs comparing CAS and CEA in symptomatic patients) demonstrate that increased age is an independent predictor of adverse CAS outcomes.[48, 49] This may be due to more advanced atherosclerotic disease with age and carotid vessels being more tortuous. Accessing the common carotid artery may be technically challenging, causing distal plaque embolisation and subsequent stroke or death.

A learning curve also exists in acquiring skills to perform CAS. The Pro-CAS registry[47] demonstrated a positive volume-outcome relationship: in centres performing under 50 CAS procedures annually, the stroke/death rate was higher compared with centres performing more than 150 CAS procedures annually. A similar relationship was demonstrated in the Stent-Protected Angioplasty versus Carotid Endarterectomy-1 (SPACE-1) study[50]: centres performing less than 50 CAS procedures annually had a higher stroke/death rate compared to centres performing more than 50 CAS procedures annually. This was supported by the Carotid Stenting Trialists' Collaboration[51] (CSTC) who pooled data from 3 RCTs: the Endarterectomy Versus Angioplasty in patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial[52], SPACE-1[53] and the International Carotid Stenting Study (ICSS).[54] Procedural stroke/death was higher in patients treated by Interventionalists performing less than 6 CAS procedures annually.[51]

CEA in Symptomatic patients

The European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) demonstrated CEA reduces stroke risk in symptomatic patients with carotid artery stenosis (Table 1.2).[55, 56] Pooled analyses from RCTs comparing CEA against CMT showed that CEA reduced stroke risk in patients with symptomatic carotid artery stenosis of 50-99% (NASCET method).[57, 58] CEA was more effective for 70-99% carotid artery stenosis than 50-69% stenosis and ineffective in stenoses less than 50%.[57-60]

Subgroup analyses demonstrated that older patients with 50-99% symptomatic carotid artery stenosis derived greatest benefit from CEA.[58] Females also derived less benefit from CEA than males.[61] However, this is likely due to underpowered subgroup analysis and a higher rate of procedural complications in females undergoing CEA in RCTs (although this was not apparent in large registry data). In clinical practice, female gender is not a barrier to undergoing CEA.

Table 1.2: CEA in long-term stroke prevention in symptomatic patients.

RCT	Years of Recruitment	Degree of Stenosis	Number of Patients	Follow-up (years)	Findings
ECST	1981-1994	≥80%	574	6.1	*Ipsilateral stroke or perioperative death* CEA: 6.8%, CMT: 20.6%; **p<0.0001**
NASCET	1987-1991	≥70%	659	1.5	*Ipsilateral stroke* CEA: 9.0%; CMT: 26.0%; **p<0.001**
	1987-1996	50-69%	858	5.0	*Ipsilateral stroke* CEA: 15.7%, CMT: 22.2%; **p=0.05**

Abbreviations – CEA: Carotid Endarterectomy; CMT: Contemporary Medical Therapy; ECST: European Carotid Surgery Trial; NASCET: North American Symptomatic Carotid Endarterectomy Trial; RCT: Randomised Clinical Trial.

Timing of CEA

Evidence suggests expediting surgery in neurologically stable patients following minor stroke because early recurrent stroke risk is high.[62-64] Up to 40% of recurrent strokes occur within 24 hours of the initial event[65] and, by 14 days, stroke risk may be 25%.[66] Early CEA may reduce recurrent stroke risk by 80%.[67] CEA should be performed within two weeks of the index event in patients with 50-99% carotid artery stenosis as it was shown to be significantly beneficial over CMT during this time, especially in males.[58, 61, 68] Benefit from CEA decreased substantially if surgery was delayed by more than two weeks after initial symptoms.[61] Another study reported that delaying CEA from 14 to 30 days after initial symptoms caused 11 more strokes per 1,000 patients[69] whilst a systematic review did not report increased risk from early surgery compared to delaying CEA in neurologically stable patients.[70]

CEA in Asymptomatic patients

RCTs comparing CEA versus CMT in asymptomatic patients include the Veterans Affairs Cooperative Study (VACS), the Asymptomatic Carotid Atherosclerosis Trial (ACAS) and the Asymptomatic Carotid Surgery Trial-1 (ACST-1), randomising patients between the 1980s and early 2000s (Table 1.3).[71-73] VACS[71] (n=444) reported a 61% reduced risk of ipsilateral neurological events after CEA compared to CMT in patients with a mean follow-up of almost 4 years. ACAS[72] (n=1,662) reported that CEA reduced the 5-year risk of the combined endpoint of ipsilateral stroke and any peri-operative stroke/death by 53% compared to CMT. ACST-1[73] (n=3,120) reported a significant reduction in stroke risk (when including peri-operative risks) at 5 and 10 years, favouring CEA over CMT.[74] This stroke risk reduction was improved when peri-operative events were excluded and half the reduction was in disabling and fatal strokes.[74]

Table 1.3: CEA in long-term stroke prevention in asymptomatic patients.

RCT	Years of Recruitment	Degree of Stenosis	Number of Patients	Follow-up (years)	Findings
VACS	1983-1987	≥50%	444	4.0	*Ipsilateral TIA, amaurosis fugax or stroke* CEA: 8.0%, CMT: 20.6%; **p<0.001**
ACAS	1987-1993	≥60%	1,662	2.7	*Peri-procedural stroke or death, and post-operative ipsilateral stroke* CEA: 5.1%, CMT: 11.0%; **p=0.004**
ACST-1	1993-2003	≥60%	3,120	5.0	*Any stroke or peri-operative death* CEA: 6.9%, CMT: 10.9%; **p=0.0001**
				10.0	*Any stroke or peri-operative death* CEA: 13.4%, CMT: 17.9%; **p=0.009**

Abbreviations – ACAS: Asymptomatic Carotid Atherosclerosis Trial; ACST: Asymptomatic Carotid Surgery Trial; CEA: Carotid Endarterectomy; CMT: Contemporary Medical Therapy; RCT: Randomised Clinical Trial; VACS: Veteran Affairs Cooperative Study.

CEA compared to CAS: Symptomatic patients

EVA-3S[52] (n=527) was stopped prematurely as the 30-day stroke/death rate was significantly higher for patients treated with CAS versus CEA. This difference remained significant at 6 months.[52] At 5 years[75], the composite endpoint of any ipsilateral stroke or procedural stroke or death remained significantly higher for CAS than CEA-treated patients.

SPACE-1[53] (n=1,214) reported no significant differences between CAS and CEA in the composite endpoint of ipsilateral ischaemic stroke or death at 30 days post-procedure or 2 years.[76] However, recurrent stenosis was more common in CAS-treated patients and older age (over 68 years) was associated with adverse outcomes at 2 years.[76]

ICSS[54] (n=1,713) reported that the incidence of procedural stroke, death or MI was significantly higher following CAS than CEA, both at 30 and 120 days. This was especially marked for any stroke and all-cause death.[54] The ICSS authors[54] performed a meta-analysis, combining data from EVA-3S[52], SPACE-1[53] and ICSS[54], and reported a 73% increased risk of 30-day stroke, death or MI following CAS compared to CEA.[54] The incidence of any stroke was more common after CAS than CEA at 5 years, due to a higher incidence of non-disabling strokes and contralateral carotid or vertebrobasilar strokes.[77]

The Carotid and Vertebral Artery Transluminal Angioplasty Study[78] (CAVATAS) reported more minor strokes lasting less than 7 days in the endovascular compared to CEA group in 504 patients (97% symptomatic). There was no significant difference in ipsilateral non-peri-operative stroke or TIA at 8 years between the endovascular cohort and patients receiving CEA.[79] However, the study was underpowered and confidence intervals (CIs) were wide.

Long-term results from these RCTs are summarised in Table 1.4.

CEA compared to CAS: Symptomatic and Asymptomatic patients

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial[80] included both symptomatic (n=96) and asymptomatic (n=237) patients. There was no significant difference in the composite endpoint of 30-day death, stroke or MI.[80] At 1 year, the CEA group had significantly more events than the CAS group.[80] This may be due to the SAPPHIRE population having greater comorbidities (75.5% of patients undergoing CEA had coronary artery disease), causing a significantly higher MI rate in the CEA compared to CAS group.[80] There was no significant difference in death or ipsilateral stroke at 3 years.[81]

The Carotid Revascularisation Endarterectomy versus Stenting Trial (CREST-1)[82] was the largest multicentre RCT comparing CEA and CAS, enrolling 1,321 symptomatic and 1,181 asymptomatic patients. Each Surgeon and Interventionalist met minimum standards for participation whilst EPDs were used in 96.1% of patients.[82] There was no significant difference in the 30-day rates of the combined endpoint of stroke, MI or death between CAS and CEA.[82] Symptom status and gender had no effect on outcomes.[82] However, stroke incidence was significantly higher following CAS than CEA and MI incidence was significantly higher after CEA than CAS.[82] This was more pronounced in symptomatic patients.[83] Strokes had a more significant impact on quality of life compared to MI and they were significantly more likely to occur in octogenarians.[84] At 4 years, there was no difference in ipsilateral stroke or death rate between CAS and CEA groups.[82] However, increased age, female sex, HTN, DM and dyslipidaemia were independent predictors of re-stenosis or re-occlusion at 2 years following CAS whilst smoking was significantly associated with re-stenosis after CEA.[85] At 10 years, there was no significant difference in the composite endpoint of stroke, MI or death and subsequent ipsilateral stroke between CAS and CEA groups, regardless of symptom status.[86]

Long-term results from these RCTs are summarised in Tables 1.4 and 1.5.

CEA compared to CAS: Asymptomatic patients

The Asymptomatic Carotid Trial-1 (ACT-1) trial[87] (n=1,453) reported that CAS was non-inferior to CEA for the composite endpoint of 30-day death, stroke or MI. Procedural death and MI was equivalent between CAS and CEA groups.[87] CEA had half the procedural stroke risk compared to CAS, though this was not statistically significant.[87] At 1 year, similar proportions of patients receiving CAS and CEA had died or experienced a stroke or MI and, by 5 years, the ipsilateral stroke rate was also comparable.[87] ACT-1 recently reported and its findings support CREST-1. However, ACT-1 and CREST-1's results may not be fully generalisable as only one type of stent and EPD was used.[82, 87] Moreover, ACT randomised patients in a 3:1 ratio to receive CAS or CEA respectively so the CEA group was small (n=364). ACT-1's long-term results are summarised in Table 1.5.

The Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis versus Carotid Endarterectomy-2 (SPACE-2) trial[88] (n=513) was designed to compare CMT alone versus CMT with CEA versus CMT with CAS. However, due to slow patient recruitment, the RCT was modified to compare CMT alone versus CMT with CEA and CMT alone versus CMT with CAS.[88] This was the first RCT to report no procedural deaths following CEA or CAS.[88] There were also no deaths or strokes within 30 days of patients being randomised to CMT whilst the combined procedural stroke/death rate was similar following CEA and CAS.[88] These results have wide CIs due to the small sample size and suggest a missed opportunity to clarify uncertainty. However, they may be pooled in a future individual patient data meta-analysis. Long-term outcomes are awaited.

Table 1.4: CAS in long-term stroke prevention, compared to CEA, in symptomatic patients. *denotes subgroup analysis

RCT	Years of Recruitment	Number of Patients	Follow-up (years)	Findings
EVA-3S	2000-2005	527	5.0	*Peri-procedural stroke, death, and post-procedural ipsilateral stroke* CEA: 6.3%, CAS: 11.0%; **p=0.04**
SPACE-1	2001-2006	1,214	2.0	*Peri-procedural stroke, death, and post-procedural ipsilateral stroke* CEA: 8.8%, CAS: 9.5%; **p=0.62**
ICSS	2001-2008	1,713	5.0	*Fatal or disabling stroke* CEA: 6.5%, CAS: 6.4%; **p=0.77**
CAVATAS	1992-1997	504	8.0	*Any stroke and peri-procedural death* CEA: 23.5%, CAS: 29.7%; **p=non-significant**
SAPPHIRE*	2000-2002	96	3.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke and death* CEA: 21.7%, CAS: 32.0%
CREST-1*	2000-2008	1,321	5.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke* CEA: 8.7%, CAS: 9.0%; **p=0.40**
			10.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke* CEA: 9.8%, CAS: 13.4%

Abbreviations – CAS: Carotid Artery Stenting; CAVATAS: Carotid and Vertebral Artery Transluminal Angioplasty Study; CEA: Carotid Endarterectomy; CREST: Carotid Revascularisation Endarterectomy versus Stenting Trial; EVA-3S: Endarterectomy Versus Angioplasty in patients with Symptomatic Severe Carotid Stenosis; ICSS: International Carotid Stenting Study; RCT: Randomised Clinical Trial; SAPPHIRE: Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; SPACE: Stent-Protected Angioplasty versus Carotid Endarterectomy.

Table 1.5: CAS in long-term stroke prevention, compared to CEA, in asymptomatic patients. *denotes subgroup analysis

RCT	Years of Recruitment	Number of Patients	Follow-up (years)	Findings
SAPPHIRE*	2000-2002	237	3.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke and death* CEA: 29.2%, CAS: 21.4%
CREST-1*	2000-2008	1,181	5.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke* CEA: 5.4%, CAS: 6.1%; **p=0.95**
			10.0	*Peri-procedural MI, stroke, death and post-procedural ipsilateral stroke* CEA: 10.1%, CAS: 9.6%
ACT-1	2005-2013	1,453	5.0	*Post-procedural ipsilateral stroke* CEA: 2.7%, CAS: 2.2%; **p=0.51**

Abbreviations – ACT: Asymptomatic Carotid Trial; CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; CREST: Carotid Revascularisation Endarterectomy versus Stenting Trial; RCT: Randomised Clinical Trial; SAPPHIRE: Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy.

CMT in Stroke Prevention

Many RCTs were instituted before advancements in modern medical therapies (e.g. statins). Most patients with carotid artery stenosis today would be prescribed a statin, anti-platelet and blood pressure modifier.[89] However, in the early years of recruitment in ACST-1[73], less than 10% of patients were taking lipid lowering therapy. This increased to 80% by the end of follow-up.[74] It has been shown that a 1 $mmol.L^{-1}$ reduction in Low Density Lipoprotein Cholesterol (LDL-C) reduces 5-year stroke risk by approximately 25%.[90-92] This might explain why statin use was associated with halving of stroke risk following CEA in ACST-1.[73, 74] However, irrespective of statin use, CEA still halved the stroke rate in ACST-1.[73, 74] Increasing statin use may have partly contributed to background stroke risk falling over recent decades. Simvastatin reduces carotid-related strokes, halving the CEA or CAS rate in symptomatic patients.[90]

Recent European Society for Vascular Surgery (ESVS) guidelines[93] recommend a healthy diet, smoking cessation and physical activity should be instituted for risk factor reduction in patients with carotid artery stenosis. Low-dose aspirin was also recommended due to its cardio-protective effects, despite its effects on preventing strokes still widely debated.[94-97] Patients intolerant of aspirin may be prescribed clopidogrel.[93] Anti-platelet therapy should be used peri-procedurally and long-term following CEA and CAS, with dual anti-platelet therapy recommended for at least 1 month post-CAS.[93]

Lipid-lowering therapy was also recommended for long-term prevention of cardiovascular disease.[93] A Cochrane review demonstrated significant reductions in all-cause mortality, fatal/non-fatal strokes and revascularisation in patients randomised to statins.[98] Atorvastatin and rosuvastatin have been prescribed in RCTs and targets of a 50% reduction in LDL-C or level less than 1.8$mmol.L^{-1}$ (70$mg.dL^{-1}$) should be achieved.[99-101] The Cholesterol Treatment Trialists' Collaboration[99] performed an individual patient data meta-analysis of 14 RCTs of

statins (including 90,056 patients) and reported a significant 12% RR reduction in all-cause mortality per mmol.L^{-1} reduction in LDL-C. There was a similar significant reduction in fatal or non-fatal stroke, with a significant 21% reduction in all major vascular events.[99] The Stroke Prevention by Aggressive Reduction in Cholesterol Levels RCT[92] also reported that atorvastatin use significantly reduced 5-year fatal or non-fatal stroke risk by 16% in 4,731 patients who had a stroke or TIA up to 6 months prior to RCT enrolment. There was a 20% reduction in the risk of major cardiovascular events.[92] More intensive lipid lowering may be possible with the use of proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors (e.g. alirocumab or evolocumab). These monoclonal antibodies, administered via subcutaneous injection every 2-4 weeks, inhibit the enzyme PCSK-9 which causes more LDL receptors to be presented to the surface of hepatocytes, increasing LDL-C metabolism. They have been shown to reduce serum LDL-C levels by 60% in patients already taking statins in RCTs.[102-104] One study compared evolocumab (in addition to statin therapy) to placebo and reported a significant 20% reduction in the hazard ratio (HR) of cardiovascular death, MI or stroke in 27,564 patients with prior cardiovascular disease.[104] Ischaemic stroke was also significantly reduced.[104] Follow-up was for 4 years so efficacy and safety of PCSK-9 inhibitors beyond this time are unknown. Their effects in patients with asymptomatic carotid artery stenosis are also uncertain but these agents may further reduce long-term stroke risk. However, they are currently used infrequently due to being very expensive.

Observational data demonstrate an association between elevated systolic blood pressure and increased stroke risk. However, the Systolic Blood Pressure Intervention Trial failed to demonstrate a significant reduction in strokes in asymptomatic patients with systolic blood pressure below 120mmHg compared to those below 140mmHg.[105] Intensive blood pressure treatment was significantly associated with hypotension and impaired renal function, compared to standard treatment.[105] Overly intensive blood pressure reduction may have deleterious

effects in patients with carotid artery stenosis who may depend on their systemic vascular resistance for brain perfusion. However, treatment of HTN is associated with reduction and regression of carotid plaques in asymptomatic patients.[106] A meta-analysis reported reduced stroke risk proportional to lowering of systolic blood pressure and a Chinese RCT demonstrated reduced stroke risk with use of enalapril.[107, 108] The pharmacological agent used is less important than achieving the blood pressure target below 140/90mmHg in non-diabetic, asymptomatic patients.[109] In diabetic patients, intensive blood pressure control reduced the RR of stroke by 44% compared to patients with a higher blood pressure.[110] Therefore, the European Society of Hypertension/European Society of Cardiology (ESC) guidelines recommend that blood pressure in diabetic patients with asymptomatic carotid artery stenosis should be below 140/85mmHg.[111] Tight glycaemic control is also recommended as these patients are at increased stroke risk.[112] In a study of Type II DM patients, use of lipid-lowering therapy, anti-platelet agents and anti-hypertensive medications was associated with a 60% reduction in cardiovascular events and deaths.[113]

Procedural Considerations

Unlike CMT, where compliance with the medication regimen tends to be poorer in clinical practice than RCTs and can reduce its effectiveness, this is not the case with interventions. However, over time, familiarity and experience has increased with surgical techniques and catheter-based procedures so carotid interventions are now safer than previously. Continually improving CMT, patient selection with pre-procedural optimisation and technological advancement will likely improve future CEA and CAS outcomes. Improvements in stent design (e.g. micro-mesh covered stents), delivery systems (e.g. trans-carotid arterial revascularisation (TCAR)) and EPDs may further reduce CAS complications.

CEA outcomes are also improved when patients are operated on by Vascular Surgeons compared to Cardiothoracic Surgeons, General Surgeons or Neurosurgeons[114-120], reflecting increased familiarity as Vascular Surgeons perform CEAs more frequently than other Specialists. A positive volume-outcome relationship in CEA also reduces stroke/death.[121] However, Vascular Surgeons, Interventional Radiologists, Neurosurgeons and Interventional Neuroradiologists performed CAS in CREST-1[82], with Vascular Surgeons having worse CAS outcomes than Interventional Radiologists, Interventional Neuroradiologists or Interventional Cardiologists.[122] This may reflect varying case complexity between specialties or lack of experience with catheter-based procedures in some specialties at the time of CREST-1.

Use of EPDs may reduce the procedural stroke rate following CAS. A systematic review[123] reported reduced 30-day stroke/death in patients undergoing CAS with EPD use. Data from a large registry[124] also confirmed EPDs reduce stroke/death rate in patients undergoing CAS, with EPD use being an independent protective factor. Varying EPD use in RCTs should therefore be considered when interpreting findings.

As CEA and CAS are prophylactic interventions, a balance needs to be made between the initial procedural hazard and long-term stroke risk reduction. It takes approximately 4 years for the benefits of intervention to exceed the protective effects of CMT in asymptomatic patients. Life expectancy is therefore required to exceed this period to justify intervention in these patients whose absolute long-term stroke risk is low. This provides the rationale for ESVS and ESC guidelines recommending a life expectancy of 5 years as a prerequisite for performing carotid interventions in asymptomatic patients.[93, 125] Those expecting to live for 10 or more good quality years may have even greater absolute gains from carotid intervention.

Future Perspectives for Asymptomatic patients

ESVS[93] and ESC guidelines[125] recommend asymptomatic patients with average surgical risk and carotid artery stenosis of 60-99% should be considered for CEA in the presence of one or more characteristics associated with increased risk of late ipsilateral stroke. Imaging/clinical criteria include: silent infarction on Computerised Tomography (CT); stenosis progression; large plaque area; plaque echolucency; intra-plaque haemorrhage on Magnetic Resonance Imaging (MRI); impaired cerebral vasoreactivity; spontaneous embolisation on Transcranial Doppler Ultrasound; and/or history of contralateral TIA.[93, 125] CAS is an alternative in these patients.[93, 125] However, in selected asymptomatic patients who are high-risk for surgery with carotid artery stenosis of 60-99%, CAS is indicated.[93, 125] Again, these patients are required to have increased risk of late ipsilateral stroke.[93, 125] Requirement for intervention is a documented procedural risk of stroke/death less than 3% and life expectancy exceeding 5 years.[93, 125] ESC guidelines have reduced their threshold for CEA and CAS complications from 6% to 3%, in line with ESVS guidelines.[101, 125]

These guidelines are based on RCT findings which may not be generalisable to contemporary practice due to use of antiquated CMT, heterogeneous patients, different endpoints used in RCTs, a variety of endovascular devices used between RCTs, varying EPD use and varied endovascular experience of Interventionalists. There is therefore uncertainty regarding which technique is superior or if CMT advancements have replaced the need for carotid intervention.

A threshold of 3% for procedural complications in asymptomatic patients may be too high. A meta-analysis reported that the combined stroke/death rate following CEA in asymptomatic patients had halved since 2005 ($p<0.001$) but, in contrast, CAS outcomes remained similar ($p=0.628$).[126] With greater experience and improvements in procedural developments (e.g. micro-mesh covered stents, TCAR), CAS procedural complication rates may fall further.

Insights from RCTs

Ongoing RCTs such as the Carotid Revascularisation and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2) and ECST-2 will compare CAS (with use of EPDs) and, separately, CEA with CMT in asymptomatic patients with severe carotid artery stenosis whilst the Endarterectomy Combined with Optimal Medical Therapy (OMT) versus OMT Alone in Patients With Asymptomatic Severe Atherosclerotic Carotid Artery Stenosis at Higher-than-average Risk of Ipsilateral Stroke Trial will compare CEA, with CMT, versus CMT alone.[127, 128] Direct comparisons between CEA and CAS will not be performed.

As part of CMT in CREST-2, participants receive intensive anti-hypertensive and lipid-lowering therapies, including PCSK-9 inhibitors.[129] Goal-directed therapy targets[130] include systolic blood pressure below 140mmHg and LDL-C less than 70mg.dL^{-1}. Participants are also enrolled in a lifestyle modification programme (INTERVENT) that targets weight loss, smoking cessation, increased exercise, reduced alcohol intake and DM management.[129] A lifestyle coach contacts them regularly by telephone (every 2 weeks for 3 months, then every 3 months until 1 year, then 6-monthly until 4 years) to ensure adherence.[129] This will better define the effect of CMT on stroke risk in asymptomatic patients (though it may not be feasible to apply this resource-intensive programme to clinical practice).[131]

ACST-2[132] will directly compare CAS with CEA for long-term stroke prevention in asymptomatic patients with severe carotid artery stenosis on CMT. ACST-2[132] is the largest RCT ever performed comparing CAS with CEA and should provide reliable evidence as it is being conducted internationally with experienced collaborators and high-quality CMT in addition to modern carotid revascularisation strategies.

The results of these RCTs are eagerly anticipated in the 2020s as they will provide clarity, in large numbers of patients (whilst also providing an opportunity for meta-analysis), regarding the effect of the increased use of statins, new stent designs and safer CAS techniques compared with CEA and CMT to better inform the management of patients with asymptomatic carotid artery stenosis.[133]

Thesis Overview

This introductory chapter has highlighted important themes that will be developed throughout the thesis. Associations between the structure of a healthcare system and procedural outcomes following carotid intervention will be further explored in a systematic review presented in Chapter 2. This will be followed by an observational study (Chapter 3) which will identify points of harm in the CEA pathway of symptomatic patients. An healthcare failure mode and effect analysis (HFMEA) will be conducted in Chapter 4 which will aim to incorporate safeguards into the clinical pathway to prospectively mitigate against harm occurring. Chapter 5 will present a study that uses administrative data to assess procedural CEA and CAS outcomes before Chapters 6 and 7 will explore how the provision of carotid interventions and procedural outcomes vary temporally and regionally throughout England, whilst also identifying factors that affect procedural and long-term CEA and CAS outcomes in Hospital Episode Statistics (HES) data. Pertinent points will be discussed and recommendations for future work suggested in light of limitations in Chapter 8.

Thesis Aims

The primary objective of this research project is to identify how the carotid intervention pathway can be improved. The aims will be three-fold:

1. Identify hospital-level structural factors that affect CEA and CAS procedural outcomes by performing a systematic review of the published literature;
2. Identify points of harm in the CEA pathway for symptomatic patients by performing an ethnographic observational study prior to undertaking HFMEA – a technique that prospectively incorporates safeguards into the clinical pathway to reduce harm by preventing adverse events;
3. Use HES data to assess how CEA and CAS provision and procedural outcomes have changed over time, identify regional variation within England and the effects of gender, degree of deprivation, ethnicity and comorbidities on procedural and long-term outcomes following carotid intervention.

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CHAPTER 2: Identifying Hospital-level Structural Factors that Improve Outcomes following Carotid Interventions: Results of a Systematic Review

Abstract

Background: Carotid endarterectomy (CEA) and carotid artery stenting (CAS) reduce long-term stroke risk but are potentially hazardous. This study aimed to examine the evidence that hospital-level structural factors affect CEA and CAS procedural outcomes.

Methods: A systematic review was conducted of studies from 2005 onwards, using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Structural factors assessed were: population size served by the vascular unit; number of hospital beds; availability of vascular beds; impact of established clinical pathways; Surgical Intensive Care Unit (SICU) size; and specialty of Surgeons/Interventionalists. Primary procedural outcomes were: stroke/death; mortality; stroke; cardiac complications; hospital length of stay (LOS); and cost.

Results: Seventeen studies from six countries were included (totalling 124,958 patients).

Vascular units serving larger populations (>75,000 people) were associated with reduced CEA mortality ($p<0.0001$) and stroke rates ($p=0.001$), compared with those serving smaller populations. Larger hospitals were associated with reduced CEA mortality ($p<0.0001$), strokes ($p=0.0008$) and cardiac events ($p=0.01$), compared with smaller hospitals (up to 130 beds).

Provision of vascular beds was associated with reduced CEA mortality ($p=0.0008$) and cardiac events ($p=0.03$). Established pathways of care were associated with reduced stroke and cardiac event rates ($p=0.004$) and CEA costs.

Large SICUs (≥7 beds) were associated with decreased mortality ($p<0.0001$) and stroke rate ($p=0.001$) compared with smaller units, whilst the presence of an Intensivist was associated with reduced mortality ($p=0.0002$) following CEA.

Patients treated by Vascular Surgeons (compared to Neurosurgeons, Cardiothoracic Surgeons and General Surgeons) were associated with significantly lower stroke/death and stroke rates, and shorter LOS, following CEA.

CAS outcomes were not influenced by Interventionalist's specialty but was significantly cheaper when performed by Vascular Surgeons ($p<0.0001$).

Conclusions: Structural factors significantly affect CEA procedural outcomes, with limited data on CAS. These findings may improve configuration of vascular services and help reduce CEA and CAS risks and costs.

Introduction

This chapter will examine the evidence that structural factors affect CEA and CAS procedural outcomes.

Evidence-Based Medicine (EBM)

EBM was defined by Sackett *et al*.[1] as the "conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients". However, critical appraisal of evidence is crucial before informing treatment decisions and involves considering its validity, reliability and relevance. Flawed studies with biased findings should be given less emphasis than well conducted studies with rigorous methodologies. An EBM approach may therefore improve quality of care and reduce healthcare costs.

Importance of EBM

Applying EBM allows investment in treatments that are both clinically and cost-effective. The National Institute for Health and Clinical Excellence combine the principles of EBM with economic analyses to recommend which treatments should be NHS-funded. This influences Primary and Secondary care. Application of EBM also allows Clinicians to choose appropriate treatment options based on patients' risk profiles and comorbidities. This is particularly important in deciding on carotid interventions where potentially hazardous treatments can be avoided in some patients.

Levels of Evidence

Evidence can be ranked based on its potential for bias. Various classification systems exist but each agree on the hierarchy used by the Scottish Intercollegiate Guidelines Network[2] for grading evidence. The highest form of evidence is a high-quality meta-analysis or systematic review of well conducted RCTs (Level 1++).[2] This is followed by high-quality systematic reviews of case-control or cohort studies (Level 2++).[2] Well conducted case-control or cohort studies are classed as Level 2+ evidence whilst case reports and case series are Level 3.[2] Expert opinion is Level 4 evidence.[2] This system allows evidence to be appraised and compared to select appropriate treatments for patients or commissioning of services. This is relevant to vascular patients as they are highly co-morbid and high-risk for complications following carotid interventions. Moreover, running Vascular Surgery services is expensive so allocating funds for effective and appropriate treatments is important.

Rationale for Study

Systematic reviews allow identification, appraisal and synthesis of published information on a topic, aiding clinical decision-making. This is valuable as they summarise all evidence on a topic, in a reproducible way. However, if their methodology is flawed or biased, their conclusions should be interpreted with caution.

The volume of studies on a given topic can be overwhelming. Systematic reviews provide high-quality, concise summaries of the evidence.[3] Moreover, individual studies may have conflicting results, leading to erroneous misinterpretations causing patient safety issues.[3] Combining studies increases statistical power, allowing more reliable conclusions to be formed.[3]

Systematic reviews also follow a pre-determined protocol, eliminating selection bias of included studies and minimising the influence of personal beliefs. They also increase the sample size for analysis, allowing a more precise estimate of treatment effect by meta-analysis.[3, 4] This strength was highlighted when the benefits of intravenous streptokinase (a thrombolytic agent) following acute MI were under-estimated in smaller RCTs and reviews by clinical experts, delaying its introduction by 20 years until larger RCTs were performed and rigorous systematic reviews with meta-analyses confirmed its effectiveness as a treatment.[5, 6] This may have caused harm to patients and emphasises the need to pool findings from studies to accurately determine treatment effect in a large number of patients. This is particularly valuable when there is uncertainty regarding a topic, such as the effect of structural factors on procedural outcomes following carotid intervention. A systematic review has recently been published examining the volume-outcome relationship in carotid intervention[7] so this study focuses on other factors.

Aim

This study aimed to summarise the evidence relating to the impact of structural factors (population size served by the vascular unit; number of hospital beds; availability of vascular beds; established clinical pathways; Surgical Intensive Care Unit (SICU) size; and specialty of Surgeons/Interventionalists) on procedural outcomes (rates of stroke/death; mortality; stroke; MI/cardiac events; LOS; and cost) following CEA and CAS.

Methods

This systematic review is reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist[8] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO) prospectively (registration number: CRD42017081202).[9]

Search Strategy

Medical Literature Analysis and Retrieval System Online (MEDLINE), using the Ovid interface from 1946 onwards, and Excerpta Medica Database (EMBASE) from 1974 onwards, were searched (initially: 08 November 2017; re-searched: 31 July 2019). Hand-searches of key journals, conference proceedings and reference lists of included titles were also conducted. Studies published before 2005 were excluded as these findings were not deemed relevant to current practice. This is similar to a recent systematic review's methodology.[10] Abstracts, review articles, case reports, editorials, opinions and commentaries were also excluded.

The search strategy is detailed in Figure 2.1 below (after consultation with a librarian).

“intensive care” OR “vascular surgeon” OR “Resident” OR “Resident” OR “hospital based” OR structur* OR “vascular anaesthetist” OR “vascular anesthesiologist” OR “vascular intensivist” OR “vascular operating theatre” OR “vascular ward” OR “vascular bed” OR “hospital bed” OR “hospital capacity” OR “registrar” OR “ICU” OR “HDU”OR “ITU” OR “vascular operating room”

AND

“death” OR “mortality” OR “stroke” OR “myocardial infarction” OR “heart attack” OR “MI” OR “length of stay” OR “cost” OR “readmission”

AND

“carotid intervention” OR “carotid revascularization” OR “carotid endarterectomy” OR “carotid stenting” OR “carotid angioplasty”

Figure 2.1: Search strategy for inclusion of studies in this systematic review.

Study Selection

The initial search yielded 1,064 titles. Of these, 68 were not in English and 286 duplicates were excluded. A single reviewer (KG) screened 710 titles. These were ratified by a second reviewer (PC), yielding 46 studies. Abstracts of these studies were independently screened by two reviewers (KG and DM), the latter was unrelated to the study and both were blinded to the other's results. There was a 91.3% agreement between KG and DM (κ=0.81; $p<0.00001$). Disagreements were adjudicated by a third reviewer (PC), yielding 16 studies for full paper review. Two papers were unavailable and two studies were deemed irrelevant and subsequently excluded. Five further studies were included after a search of the reference lists of included papers. Figure 2.2 summarises the whole process. These 17 papers were read independently by two reviewers (KG and PC). Data were extracted and the quality of each study was assessed and documented on a pre-prepared *pro forma* (Appendix I).

Data Collection

Data extracted included: authors; year of publication; years study was conducted; country of investigation; study design; type of intervention; number of centres; number of patients; symptom status; risk factor assessment; structural factor(s) assessed; and procedural outcomes.

Structural factors assessed included: population size served by the vascular unit; number of hospital beds; availability of vascular beds; established clinical pathways; SICU size; and specialty performing the intervention. Studies examining the volume-outcome relationship were excluded as a systematic review and meta-analysis has recently been published on this topic and its effect on both CEA and CAS procedural outcomes.[7]

Study Outcomes

Primary outcomes included: 30-day rates of stroke/death; mortality; stroke; MI/cardiac events; LOS; and cost (in United States Dollars (USD)).

Quality Assessment

Quality of studies was assessed using the Newcastle-Ottawa scale for observational studies.

A meta-analysis was not performed due to heterogeneity of included studies. Results are presented in narrative form with tabulations.

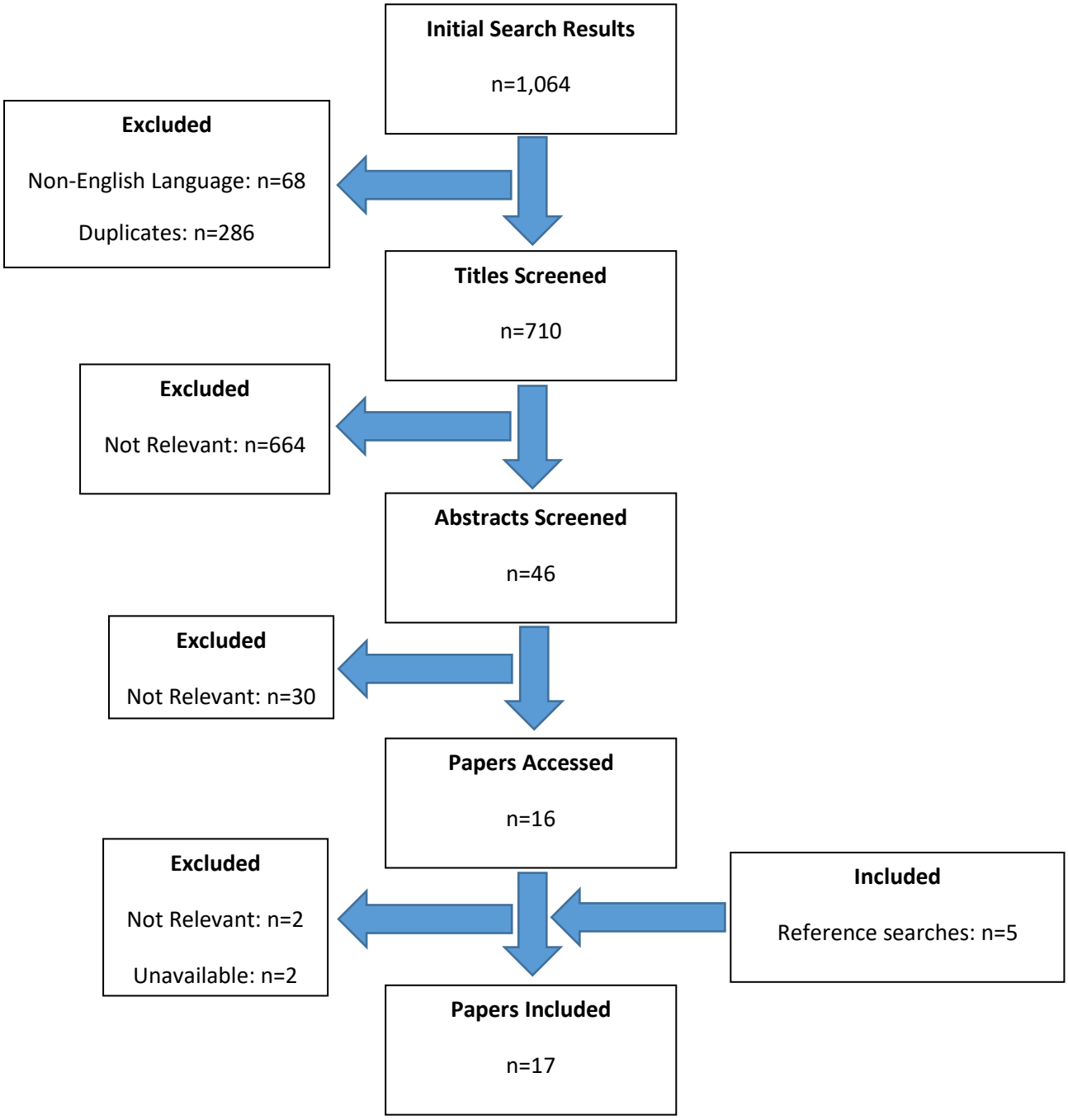

Figure 2.2: PRISMA diagram for the selection of studies in this systematic review.

Results

Study Characteristics (Table 2.1)

Seventeen studies[11-27] from six countries, totalling 124,958 patients, were included. Nine were conducted in the USA[11, 12, 15-17, 22-24, 27], one in Canada[18], one in both the USA and Canada[25], two in the UK[13, 26], two in Australia[14, 21], one in Germany[19] and one in Austria.[20]

CEA was analysed in all studies except two[16, 24] which examined CAS exclusively whilst one study[25] examined both CEA and CAS. Both symptomatic and asymptomatic patients were examined together in all studies, except for Gray *et al*.[16] (who examined asymptomatic patients) and Paty *et al*.[22] (who examined symptomatic patients). Three studies[13, 15, 23] did not clarify their patients' symptom status.

Quality Assessment (Table 2.1)

Nine papers[11-14, 18, 20-22, 26] reported single-centre studies and the quality varied from zero to seven stars on the Newcastle-Ottawa Scale. There were six[15, 18, 23-25, 27] medium quality studies (7 stars) whilst the remaining eleven[11-14, 16, 17, 19-22, 26] were low quality (≤6 stars).

All studies were retrospective, except Cantlay *et al*.[13] (cross-sectional study).

Table 2.1: Characteristics of included studies. Quality was assessed by the Newcastle-Ottawa Scale for Observational Studies.

Authors	Year of Publication	Years Included in Study	Country/ Countries	Study Design	Intervention(s)	Number of Centres	Sample size	Symptomatic/ Asymptomatic	Quality
Abu Rahma *et al.*	2014	Not stated	USA	Retrospective	CEA	1	1,000	Both	****
Abu Rahma *et al.*	2013	2010-2011	USA	Retrospective	CEA	1	953	Both	******
Cantlay *et al.*	2006	2002-2004	UK	Cross-sectional	CEA	1	87	Not stated	0
Chen *et al.*	2016	2008-2009 & 2011-2012	Australia	Retrospective	CEA	1	117	Both	*****
Enomoto *et al.*	2014	2005-2010	USA	Retrospective	CEA	Not stated	34,493	Not stated	*******
Gray *et al.*	2011	2006-2009	USA	Retrospective	CAS	180	3,388	Asymptomatic	*****
Hollenbeak *et al.*	2010	1995-2002	USA	Retrospective	CEA	Not stated	17,627	Both	*****
Hussain *et al.*	2018	2002-2015	Canada	Retrospective	CEA	1	16,544	Both	*******
Lutz *et al.*	2009	1995-2004	Germany	Retrospective	CEA	2	1,379	Both	******
Metzger *et al.*	2014	2002-2011	Austria	Retrospective	CEA	1	1,452	Both	******
Organ *et al.*	2008	1992-2007	Australia	Retrospective	CEA	1	1,313	Both	*****
Paty *et al.*	2014	2002-2012	USA	Retrospective	CEA	1	369	Symptomatic	*****
Reeves *et al.*	2012	2005-2009	USA	Retrospective	CEA	>200	25,280	Not stated	*******
Steppacher *et al.*	2009	2005-2006	USA	Retrospective	CAS	424	4,001	Both	*******
Timaran *et al.*	2013	2000-2008	USA & Canada	Retrospective	CAS & CEA	117	2,320	Both	*******
Walsh *et al.*	2010	2003-2007	UK	Retrospective	CEA	1	347	Both	******
Westvik *et al.*	2006	1991-2002	USA	Retrospective	CEA	26	14,288	Both	*******

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; UK: United Kingdom; USA: United States of America.

Population Size, Bed Capacity and Availability

Westvik *et al*.[27] examined the effect of population size, bed capacity and availability on CEA outcomes. Vascular units serving larger populations (defined as >75,000 people in the study) were associated with significantly reduced mortality (0.4% versus 0.9%; p<0.0001) and total stroke rate (1.0% versus 1.8%; p=0.001) following CEA than those serving smaller populations but there was no effect on MI/cardiac event rate (2.5% versus 2.2%; p=0.32).[27]

There was also significantly reduced mortality rate after CEA associated with increasing hospital bed capacity (p<0.0001).[27] Compared to the highest level of bed capacity (≥280 beds), the lowest level (≤131 beds) was associated with a statistically significant odds ratio (OR) for mortality (OR: 2.78 (1.10-7.04); p=0.03).[27] There was a similar inverse trend for total stroke rate (p=0.0008) with the OR for the lowest level of bed capacity being 1.96 (1.32-2.90); p=0.001.[27] Increasing hospital bed capacity was also associated with significantly reduced MI/cardiac event rate (p=0.01) following CEA, with the lowest (OR 3.01 (1.45-6.24); p=0.003) and middle (OR 2.15 (1.08-4.28); p=0.03) levels of bed capacity having significantly elevated rates of MI/cardiac events compared to the highest level of bed capacity.[27]

Availability of vascular beds was associated with significantly reduced mortality (0.2% versus 0.6%; p=0.0008) and MI/cardiac event rate (OR 1.35 (1.03-1.76); p=0.03) following CEA but had no effect on total stroke rate (p=0.72).[27]

Established Clinical Pathway

Three studies[14, 22, 27] examined the impact of an established clinical pathway on CEA outcomes. There was no difference in mortality between groups with and without a pathway.[22, 27] However, Paty *et al*.[22] described a total stroke rate of 3.1% amongst pathway patients and 7.9%

in non-pathway patients (p=0.03) following CEA, caused by higher rates of minor stroke (3.4% versus 2.1%) and disabling/major stroke (3.4% versus 1.0%) amongst non-pathway patients than those with an established pathway respectively. Similarly, Westvik *et al*.[27] reported a significantly lower total stroke rate associated with patients who had a pathway than those without (1.0% versus 1.5%; p=0.01) after CEA.

Patients with an established pathway were also associated with significantly lower MI/cardiac event rates following CEA than those without (2.0% versus 2.7%; p=0.004)[27] and using a clinical pathway saved $616.73 USD per patient.[14]

SICU Care

One study[27] examined the effect of various aspects of the Intensive Care Unit (ICU) on CEA outcomes. Larger ICUs (≥7 beds) were associated with significantly lower mortality (0.3% versus 0.8%; p<0.0001) and stroke rates (1.1% versus 1.7%; p=0.001) following CEA than smaller ICUs.[27] However, ICU size had no effect on MI/cardiac event rate (p=0.46).[27]

Westvik *et al*.[27] also reported that SICUs were associated with reduced mortality by more than half following CEA compared to mixed ICUs (0.3% versus 0.7%; p=0.002), which admitted both surgical and medical patients. A higher total stroke rate following CEA was also significantly associated with mixed ICUs than SICUs (1.5% versus 1.0%; p=0.01).[27] However, MI/cardiac event rate was similar in both settings (p=0.60).[27]

Selective ICU admission (based on pre-determined criteria) was associated with halving of the mortality rate compared to routine post-operative admission (0.3% versus 0.6%; p=0.01) but did not affect total stroke (p=0.63) or MI/cardiac event rates (p=0.67) following CEA.[27]

The presence of an Intensivist was associated with an almost 3-fold reduced mortality (0.4% versus 1.1%; p=0.0002) following CEA whilst total stroke rate was non-significantly reduced (1.2% versus 1.7%, p=0.12).[27] MI/cardiac event rate was similar between groups with and without designated Intensivists (p=0.65).[27]

Vascular Anaesthetist

Two studies reported CEA mortality rates of 0.6% and 1.1% following Vascular Anaesthetic input[13, 26] whilst one study[13] reported a total stroke rate of 2.3% following pre-assessment.

Specialty Performing CEA

Six studies[11, 12, 15, 17, 18, 25] examined the effect of various specialties on CEA outcomes. Abu Rahma *et al.*[12] initially reported no significant differences in 30-day outcomes between CEA performed by Vascular Surgeons, Cardiothoracic Surgeons or General Surgeons. However, in a study with a larger sample size, Abu Rahma *et al.*[11] reported that Vascular Surgeons were associated with significantly reduced combined stroke/death rates than non-Vascular Surgeons (1.3% versus 3.1%; p=0.05) following CEA.

No study reported a significant difference in 30-day mortality between Vascular or non-Vascular Surgeons performing CEA (although Vascular Surgeons had better outcomes generally). However, Hussain *et al.*[18] reported a significantly higher 30-day rate of stroke/death post-CEA associated with Cardiothoracic Surgeons (4.4%; p=0.03) and Neurosurgeons (4.1%; p=0.05) compared to Vascular Surgeons (2.9%). Despite General Surgeons having similar outcomes to Vascular Surgeons, the overall non-Vascular Surgical group was associated with significantly increased risk of 30-day mortality and stroke than the Vascular Surgical group

(p=0.008).[18] This was supported by Timaran *et al*.[25] and the effect appears to be driven by increased 30-day total stroke risk. Enomoto *et al*.[15] reported significantly increased 30-day total stroke risk after CEA associated with General compared to Vascular Surgeons (2.4% versus 1.6%; p=0.01) whilst Hussain *et al*.[18] reported similarly worse outcomes in Cardiothoracic (4.2%; p=0.03) and Neurosurgical (3.8%; p=0.009) groups compared to Vascular Surgeons (2.5%). This effect persisted when non-Vascular Surgeons were compared with Vascular Surgeons (OR: 1.38 (1.11-1.71); p=0.004).[18] However, 30-day minor stroke rates following CEA were similar between Vascular, Cardiothoracic and General Surgeons.[12] Vascular Surgeons were associated with significantly higher 30-day MI/cardiac event rates following CEA than General Surgeons (0.7% versus 0.2%; p=0.02).[15, 25]

LOS after CEA was similar between Vascular and General Surgical groups in one study[15] but significantly longer in the General Surgical group in an older study (p=0.0001).[17] Similarly, CEAs performed by Vascular Surgeons were more than $1,000 USD cheaper than the Cardiothoracic/General Surgical group in one study[11] but significantly more expensive compared to the General Surgical group in an older study (p=0.0001).[17]

Specialty Performing CAS

Three studies[16, 24, 25] examined the effect of various specialties on CAS outcomes. Similar rates of procedural mortality, stroke/death, total stroke, 30-day minor stroke, disabling/major stroke and MI/cardiac events were reported for Interventional Cardiologists, Interventional Neuroradiologists, Interventional Radiologists, Neurosurgeons and Vascular Surgeons performing CAS.[16, 24, 25] LOS was also comparable between Vascular Surgical (2.8 days) and non-Vascular Surgical groups (3.0 days) whilst CAS performed by Vascular Surgeons was significantly cheaper compared to non-Vascular Surgeons (p<0.0001).[24]

Trainee Performing CEA

Five studies[19-21, 23, 27] examined the effect of a Trainee performing CEA on procedural outcomes. Higher mortality rates were associated with Consultants performing CEA than Trainees in some studies.[19, 27] Westvik *et al*.[27] reported a 3-fold higher procedural mortality associated with CEA performed by Consultants compared to Trainees (0.9% versus 0.3%; p<0.0001) but combined stroke/death rates were comparable in other studies.[20, 21] However, when Trainee operating was subdivided into the trainer being scrubbed or unscrubbed, there was a significantly higher stroke/death rate associated with the unscrubbed group compared to Consultants (3.7% versus 2.3%; p=0.03).[21]

Total stroke rate following CEA was similar between Consultants and Trainees[19], with a trend for Consultants having higher stroke rates.[23] This was found to be statistically significant by Westvik *et al*.[27] (1.8% versus 1.1%; p=0.001). Metzger *et al*.[20] reported comparable, but higher, rates of minor stroke and disabling/major stroke associated with CEA performed by Consultants than Trainees. The same authors[20] and Westvik *et al*.[27] also reported similar rates of MI/cardiac events following Consultant-operated and Trainee-operated cases.

Tables 2.2, 2.3 and 2.4 summarise all above results.

Table 2.2: A summary of the effect of various structural factors on outcomes following CEA. Percentages are given to 1 decimal place; non-significant p-values, costs and odds ratios (with 95% confidence intervals) are given to 2 decimal places; and significant p-values are highlighted and given to 1 significant figure.

Structural Factor	Study (Year)	Mortality Rate	Total Stroke Rate	Minor Stroke Rate	Disabling/Major Stroke Rate	MI/Cardiac Event Rate	Cost (USD)
Population Size	Westvik *et al*. (2006)	≤75K 0.9% >75K 0.4% (**p<0.0001**)	≤75K 1.8% >75K 1.0% (**p=0.001**)			≤75K 2.2% >75K 2.5% (p=0.32)	
Hospital Bed Capacity	Westvik *et al*. (2006)	≤131 beds 1.2% 132-279 beds 0.6% ≥280 beds 0.3% (**p<0.0001**) ≤131 beds **OR 2.78 (1.10-7.04)** **p=0.03**	≤131 beds 2.2% 132-279 beds 1.4% ≥280 beds 1.1% (**p=0.0008**) ≤131 beds **OR 1.96 (1.32-2.90)** **p=0.001**			≤131 beds 3.4% 132-279 beds 2.3% ≥280 beds 2.2% (**p=0.01**) ≤131 beds **OR 3.01 (1.45-6.24)** **p=0.003** 132-279 beds **OR 2.15 (1.08-4.28)** **p=0.03**	
Vascular Beds	Westvik *et al*. (2006)	Vascular beds 0.2% None 0.6% (**p=0.0008**)	Vascular beds 1.2% None 1.3% (p=0.72)			Vascular beds 2.0% None 2.6% (**p=0.03**) **OR 1.35 (1.03-1.76)** **p=0.03**	
Impact of Pathway	Chen *et al*. (2016)						616.73 saving per patient
	Paty *et al*. (2014)	Pathway 0.0% No Pathway 0.0%	Pathway 3.1% No Pathway 7.9% (**p=0.03**)	Pathway 2.1% No Pathway 3.4%	Pathway 1.0% No Pathway 3.4%		
	Westvik *et al*. (2006)	Pathway 0.5% No Pathway 0.5% (p=0.90)	Pathway 1.0%, No Pathway 1.5% (**p=0.01**) **OR 1.39 (1.02-1.90)** **p=0.04**			Pathway 2.0% No Pathway 2.7% (**p=0.004**) **OR 1.50 (1.19-1.89)** **p=0.001**	

ICU Bed Capacity	Westvik *et al*. (2006)	≤6 beds 0.8% ≥7 beds 0.3% (**p<0.0001**)	≤6 beds 1.7% ≥7 beds 1.1% (**p=0.001**)	≤6 beds 2.2% ≥7 beds 2.4% (p=0.46)
Type of ICU	Westvik *et al*. (2006)	SICU 0.3% Mixed ICU 0.7% (**p=0.002**)	SICU 1.0% Mixed ICU 1.5% (**p=0.01**)	SICU 2.3% Mixed ICU 2.4% (p=0.60)
SICU Admission	Westvik *et al*. (2006)	Selective 0.3% Routine 0.6% (**p=0.01**)	Selective 1.2% Routine 1.3% (p=0.63)	Selective 2.3% Routine 2.4% (p=0.67)
Presence of Intensivist	Westvik *et al*. (2006)	Intensivist 0.4% No Intensivist 1.1% (**p=0.0002**)	Intensivist 1.2%, No Intensivist 1.7% (p=0.12)	Intensivist 2.4% No Intensivist 2.2% (p=0.65)
Effect of VA	Cantlay *et al*. (2006)	With 1.1%	With 2.3%	
	Walsh *et al*. (2010)	With 0.6%		

Abbreviations – ICU: Intensive Care Unit; MI: Myocardial Infarction; OR: Odds Ratio; SICU: Surgical Intensive Care Unit; USD: United States Dollar; VA: Vascular Anaesthetist.

Table 2.3: A summary of the effect of various Specialists performing carotid interventions on outcomes. Percentages are given to 1 decimal place; non-significant p-values, costs and odds/hazard ratios (with 95% confidence intervals) are given to 2 decimal places; and significant p-values are highlighted and given to 1 significant figure.

Structural Factor	Study (Year)	Mortality Rate	Stroke/Death Rate	Total Stroke Rate	Minor Stroke Rate	Disabling/Major Stroke Rate	MI/Cardiac Event Rate	LOS (days)	Cost (USD)
VS performing CEA	Abu Rahma *et al*. (2014)		VS 1.3% CTS 2.7% GS 4.1% (p=0.11) non-VS 3.1% (**p=0.05**)						VS 1503.53 CTS/GS 2684.04
	Abu Rahma *et al*. (2013)	VS 0.7% CTS 0.5% GS 0.0% (p=1.00) non-VS 0.7% (p=0.67)	VS 1.3% CTS 2.9% GS 4.1% (p=0.13) non-VS 3.2% (p=0.06)	VS 1.3% CTS 2.9% GS 4.1% (p=0.13) non-VS 3.2% (p=0.06)	VS 1.1% CTS 1.0% GS 0.0% (p=0.80) non-VS 0.8% (p=0.74)		VS 0.5% CTS 0.8% GS 0.0% (p=0.83) non-VS 0.6% (p=1.00)		
	Enomoto *et al*. (2014)	VS 0.7% GS 1.1% (p=0.11)		VS 1.6% GS 2.4% (**p=0.01**) **OR 1.56 (1.13-2.17)** **p=0.008**			VS 0.7% GS 0.2% (**p=0.02**) **OR 0.34 (0.12-0.90)** **p=0.03**	VS 2.7 GS 2.8 (p=0.21)	
	Hollenbeak *et al.* (2010)							VS 3.1 GS 3.5 (**p=0.0001**) CTS 3.2 NS 3.4 non-VS 3.1	VS 13,199.51 GS 12,659.87 (**p=0.0001**) CTS 12,448.30 NS 16,447.94 non-VS 13,165.04
	Hussain *et al.* (2017)	VS 0.8% CTS 0.9% (p=0.46) GS 1.2% (p=0.18) NS 0.7% (p=0.81) non-VS 0.9% OR 1.19 (0.8-1.76) p=0.40	VS 2.9% CTS 4.4% **OR 1.54 (1.04-2.30)** **p=0.03** GS 3.7% OR 1.33 (0.88-1.72) p=0.22 NS 4.1% **OR 1.27 (1.00-1.61)** **p=0.05**	VS 2.5% CTS 4.2% (**p=0.03**) GS 3.0% (p=0.33) NS 3.8% (**p=0.009**) non-VS 3.6% **OR 1.38 (1.11-1.71)** **p=0.004**					

	Timaran *et al*. (2013)		non-VS 4% (**p=0.008**) VS 1.2% ± 0.4 non-VS 3.8% ± 0.9 **HR 0.32 (0.14-0.72)** **p=0.006**				VS 2.6% non-VS 1.5%		
VS performing CAS	Gray *et al*. (2011)	VS 1.3% (0.6-2.5) IC 0.6% (0.4-1.1) IN 1.5% (0.2-5.4) IR 0.5% (0.0-2.6) NS 0.0% (0.0-7.0)	VS 3.1% (1.9-4.7) IC 2.5% (1.9-3.2) IN 3.0% (0.8-7.6) IR 2.4 (0.8-5.5) NS 3.9% (0.5-13.5)	VS 2.7% (1.6-4.2) IC 1.9% (1.4-2.6) IN 1.5% (0.2-5.4) IR 1.9% (0.5-4.9) NS 3.9% (0.5-13.5)	VS 1.5% (0.7-2.7) IC 1.4% (1.0-2.0) IN 1.5% (0.2-5.4) IR 1.9% (0.5-4.9) NS 2.0% (0.0-10.4)	VS 1.2% (0.5-2.3) IC 0.6% (0.3-1.0) IN 0.0% (0.0-2.8) IR 0.0% (0.0-1.8) NS 2.0% (0.0-10.4)	VS 0.3% (0.0-1.1) IC 0.4% (0.2-0.7) IN 0.0% (0.0-2.8) IR 0.5% (0.0-2.6) NS 0.0% (0.0-7.0)		
	Steppacher *et al*. (2009)*	VS 0.9% IC 0.5% (p=0.24) IR 0.5% (p=0.18) non-VS 0.5% (p=0.13)		VS 1.3% IC 1.1% (p=0.59) IR 2.0% (p=0.22) non-VS 1.5% (p=0.73)				VS 2.8 ± 4.2 non-VS 3.0 ± 4.9 (p=0.13)	VS 34,400.00 non-VS 40,600.00 (**p<0.0001**)
	Timaran *et al*. (2013)		VS 3.8% ± 1.2 non-VS 4.5% ± 0.7 HR 1.12 (0.54-2.35) p=0.76				VS 0.4% non-VS 0.9%		

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; CTS: Cardiothoracic Surgeon; GS: General Surgeon; HR: Hazard Ratio; IC: Interventional Cardiologist; IN: Interventional Neuroradiologist; IR: Interventional Radiologist; LOS: Length of Stay; MI: Myocardial Infarction; NS: Neurosurgeon; OR: Odds Ratio; USD: United States Dollar; VS: Vascular Surgeon.

* This study assessed in-hospital outcomes whereas all other studies examined 30-day outcomes

Table 2.4: A summary of the effect of Trainees performing CEA on outcomes. Percentages are given to 1 decimal place; non-significant p-values are given to 2 decimal places; and significant p-values are highlighted and given to 1 significant figure.

Structural Factor	Study (Year)	Mortality Rate	Stroke/Death Rate	Total Stroke Rate	Minor Stroke Rate	Disabling/Major Stroke Rate	MI/Cardiac Event Rate
Effect of Trainee	Lutz *et al*. (2009)	Consultant 0.9% Trainee 0.4%		Consultant 3.1% Trainee 3.2%			
	Metzger *et al*. (2014)	Consultant 0.3% Trainee assisting 0.2% Trainee 0.3%	Consultant 1.7% Trainee assisting 1.2% Trainee 1.4%		Consultant 1.8% Trainee assisting 1.3% Trainee 1.4%	Consultant 1.4% Trainee assisting 1.0% Trainee 1.1%	Consultant 0.7% Trainee assisting 0.4% Trainee 0.5%
	Organ *et al*. (2008)		Consultant 2.3% Trainee 2.7% (p=0.60)				
			Consultant 2.3% Trainee (STS) 2.4% Trainee (STU) 3.7% (**p=0.03**)				
	Reeves *et al*. (2012)	Consultant 0.6% Trainee 0.6%		Consultant 1.7% Trainee 1.4%			
	Westvik *et al*. (2006)	Consultant 0.9% Trainee 0.3% (**p<0.0001**)		Consultant 1.8% Trainee 1.1% (**p=0.001**)			Consultant 2.0% Trainee 2.5% (p=0.11)

Abbreviations – MI: Myocardial Infarction; STS: Supervised with Trainer Scrubbed; STU: Supervised with Trainer Unscrubbed.

Discussion

This is the first systematic review to assess the impact of structural factors on CEA and CAS procedural outcomes. The results suggest that improved CEA outcomes may be achieved when large vascular units, in large hospitals, serve large populations. Established pathways of care and large SICUs may also contribute to improve CEA outcomes. Whilst Vascular Surgeons appear to have better CEA outcomes compared to non-Vascular Surgeons, CAS outcomes are comparable between specialties. These findings highlight the need for increased emphasis on optimising structural factors due to their impact on CEA and CAS procedural outcomes. Our findings may help improve configuration of vascular services and reduce risks and costs associated with carotid interventions although data on CAS were limited.

Population Size, Bed Capacity and Availability

Vascular units serving populations greater than 75,000 people, with large numbers of hospital beds for vascular patients, were associated with significantly reduced mortality following CEA. Reduced total stroke rate following CEA was significantly associated with a larger population served and increasing hospital bed capacity whereas reduced MI/cardiac event rate was associated with increasing hospital bed capacity and availability of vascular beds. The authors[27] demonstrated a positive correlation between hospital bed capacity and CEA volume ($p<0.0001$). As the volume-outcome relationship in CEA reduces procedural stroke/death[7], this may explain why increased hospital bed capacity improved outcomes. Population size may also determine number of CEAs performed, acting as a proxy for volume, explaining its positive impact on outcomes. However, UK vascular units should serve populations greater than 800,000 people so the applicability of this study's findings may be limited.

Vascular beds might allow closer monitoring of patients by Vascular Surgeons who are more experienced in the detection and management of post-operative vascular complications than other Specialists, allowing earlier access to imaging and intervention, improving outcomes. These findings are relevant in an era of increased hospital admissions resulting in decreased surgical bed capacity and cancellations of operations. A greater priority should be given to centralisation of resources so hospitals can serve larger populations with sufficient bed capacity and availability to improve CEA outcomes.

Established Clinical Pathway

Established clinical pathways were associated with significantly reduced total stroke and MI/cardiac event rates following CEA but had no effect on mortality. This may be due to publication bias but is expected as defined protocols including Specialist Stroke Neurology input, trained Nursing staff, admission to a stroke unit with neuro-ICU, immediate access to imaging and access to rehabilitation services[22] may optimise patients for CEA, improving outcomes. An established pathway expediting transfer for cardiac angiography[27] may also reduce the MI/cardiac event rate following CEA. It is therefore unsurprising that using a pathway reduced costs.[14] This has been reported elsewhere[28] and supports the establishment of clinical pathways to streamline patient care.

SICU Care

Large SICUs (similar to UK Surgical High Dependency Units (HDUs)) were associated with decreased mortality and total stroke rate following CEA whilst the presence of Intensivists and selective SICU admissions were associated with significantly improved mortality. This is

expected as more invasive monitoring in a SICU (e.g. intra-arterial blood pressure) allows strict control of physiological parameters and early detection of complications. Moreover, increased Nurse:Patient ratio and clinical pathways improve outcomes.[22, 27] Similar findings relating to improved outcomes following ICU care have been demonstrated following Emergency General Surgery.[29, 30] However, these findings probably suggest outdated practice as routine admission to SICU following CEA is not warranted.[27, 31-35]

Specialty Performing CEA

Improved CEA outcomes were associated with patients operated by Vascular Surgeons instead of Cardiothoracic Surgeons, General Surgeons or Neurosurgeons. This finding is supported by older studies[36, 37] and might reflect that Vascular Surgeons perform CEAs more frequently than other Specialists and are more familiar with the operation. The volume-outcome relationship in CEA is established.[7]

However, no study found superiority of Vascular Surgeons for CEA mortality, with benefit largely due to reduced procedural strokes. Abu Rahma *et al*.[11] suggested this may be due to Vascular Surgeons using patch closure of arteriotomies more commonly than other Specialists. Procedural stroke rate was 1.9% after patch use but 11.1% after primary closure (p=0.007).[11]

Our finding that the MI/cardiac event rate may be higher for patients treated by Vascular Surgeons contrasts with another study[38] and might be explained by their marginally significantly higher rate of angina (p=0.04).[15] When death/stroke/MI/cardiac events were combined, patients who had their CEA performed by Vascular Surgeons were associated with significantly better outcomes than patients not treated by Vascular Surgeons (2.8% versus 3.4% respectively; p<0.001).[15] Similar results have been reported in a recent meta-analysis.[39]

As improved CEA outcomes were associated with Vascular Surgical-treated patients, they had shorter LOS than patients not treated by Vascular Surgeons.[15, 17] One study[11] reported that treatment by Vascular Surgeons saved over $1,000 USD due to increased use of Doppler Ultrasound pre-operatively whilst other specialties preferred more expensive imaging modalities. These findings suggest Vascular Surgeons should preferentially perform CEA.

Specialty Performing CAS

CAS outcomes were not influenced by the Interventionalist's specialty, in keeping with the results from a recent systematic review and meta-analysis.[39] This contrasts with findings by Hopkins *et al.*[40] who reported increased 30-day risk of death/stroke/MI associated with patients undergoing CAS by Vascular Surgeons (OR 2.05 (1.18-3.56)) in the lead-in phase of CREST-1. This may be due to differences in case complexity, familiarity with CAS at the time of the RCT or underpowered subgroup analysis causing potential statistical artefact. There was no significant difference in outcomes between Interventional Radiologists, Neurosurgeons or Interventional Neuroradiologists performing CAS in that study.[40]

Studies included in this systematic review may not have reported differences in CAS outcomes between specialties due to methodological limitations. Gray *et al.*[16] performed a subgroup analysis of an asymptomatic non-octogenarian cohort of the Carotid ACCULINK/ACCUNET Post-approval Trial to Uncover Rare Events non-randomised trial, which was neither designed nor adequately powered to compare CAS outcomes between different specialties. Steppacher *et al.*[24] under-estimated procedural stroke rate by not uniformly performing independent neurological evaluation of included patients whilst Timaran *et al.*[25] employed strict training and credentialing of Interventionalists so their results may not be generalisable.

LOS was comparable between Vascular and non-Vascular Surgical groups. Costs associated with CAS were lower in patients treated by Vascular Surgeons ($6,200 USD; p<0.0001), which may reflect Vascular Surgeons' preference for cheaper pre-procedural investigations.[24]

Trainee Performing CEA

Our finding that Trainees performing CEA were comparable in all outcomes to Consultants is similar to other studies.[41-44] Westvik *et al*.[27] reported significantly lower mortality (p<0.0001) and total stroke rate (p=0.001) following CEA associated with Trainees versus Consultants, despite significantly longer clamping time (p<0.001), operating time (p<0.001) and anaesthesia time (p<0.0001).[19, 23] This might be explained by case selection whereby Consultants chose more complex patients to operate on than Trainees. This is supported by Consultant Vascular Surgeons having a significantly larger proportion of re-do operations compared to Trainees (0.2% versus 2.5%; p=0.01)[19] and a greater proportion of American Society of Anesthesiology class 3 or above patients (p<0.0001).[23]

Trainees operating with Consultants unscrubbed were associated with significantly higher rates of stroke/death (p=0.03)[21] and intra-operative blood transfusion (p=0.01)[23] than Consultants. This suggests that vigilance is required by trainers to safeguard optimal patient outcomes.

Strengths

This is the first systematic review to assess the impact of structural factors on CEA and CAS outcomes. The study had a clear aim and followed PRISMA guidelines.[8] It was also prospectively registered with PROSPERO[9] and all relevant studies were identified by searching multiple databases (MEDLINE and EMBASE). The grey literature was also searched

in addition to hand-searches of reference lists. Quality of all studies was also assessed and data extracted and documented on a pre-prepared *pro forma*, with significant agreement between three reviewers involved in title, abstract and full paper screens ($\kappa=0.81$; $p<0.00001$).

Evidence was synthesised in a balanced, unbiased fashion with findings contextualised, making it clinically relevant. The majority of included studies also had reasonably large sample sizes and were published within the last 15 years, representing recent practice.

Limitations

This systematic review is limited by the majority of included studies being low quality and retrospective.[45] A meta-analysis could not be performed due to heterogeneity of included studies and the volume-outcome relationship was excluded because a systematic review and meta-analysis was recently published on this topic.[7] Moreover, studies based on administrative data may have coding errors.[45] However, our findings have been supported by the literature.

The effect on CEA outcomes of some structural factors (such as aspects of SICU care, bed capacity, vascular bed availability and population size) was only assessed in one study.[27] Moreover, the effect on CEA and CAS outcomes of other structural factors (such as access to imaging or MDT working) has not been examined in the literature. This systematic review has therefore identified areas for further research, with particular emphasis required on the effect of structural factors on CAS outcomes.

Studies included were from economically developed countries, limiting generalisability of findings to developing countries.[45] Moreover, comparing outcomes in studies conducted in a number of different countries may be problematic due to regional variation in the amount of

resources allocated to carotid interventions. The centres contributing to the studies are also likely to be high-volume vascular units, further limiting generalisability.[45]

Finally, all studies examined 30-day outcomes (except one[24] which assessed in-hospital outcomes).

Conclusions and Implications

This systematic review has demonstrated that structural factors significantly affect CEA procedural outcomes, although data on CAS were limited. These findings highlight the need for increased emphasis on optimising structural factors to improve the configuration of vascular services to reduce risks and costs associated with carotid interventions.

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CHAPTER 3: Identifying Harm in the Carotid Surgical Pathway in Gloucestershire and Wiltshire: a Multicentre, Ethnographic, Observational Study

Abstract

Background: Since the 1990s, our understanding of the scale of iatrogenic harm has improved but points of harm in the carotid surgical pathway remain unknown. This study aimed to identify structural factors causing harm or potential harm to symptomatic patients from neurological event until discharge following CEA.

Methods: Ethnography was used to prospectively observe the CEA pathway of consecutive patients presenting to 3 hospitals with strokes, transient ischaemic attacks (TIAs) or amaurosis fugax, between May – July 2019. The primary outcome was the number of adverse events (unintended injuries that occurred). Secondary outcomes were serious incidents and non-critical events. Serious incidents were events with the potential to cause harm (including iatrogenic causes) and non-critical episodes were incidents perceived to be inconveniencing to a patient (medical management may have been optimal).

Results: Ten patients were observed for 1,072 hours over 6 weeks. There were 110 patient safety incidents recorded where harm or potential harm may have occurred – a rate of one incident approximately every 10 hours. Of these, 10 (9.1%) were adverse events, 66 (60.0%) were serious incidents and 34 (30.9%) were non-critical. Half of patients had an adverse event between symptoms and discharge following CEA. The commonest failures were documentation, public health awareness and the environment delivering care. There were no procedural deaths, strokes or myocardial infarctions. Median delay from symptoms to surgery

was 7.5 (range: 5-40) days. Seven (70%) patients had CEA scheduled within 14 days of symptoms whilst five (50%) patients had CEA scheduled within 7 days of symptoms.

Conclusions: Various structural factors contribute to harm or potential harm in symptomatic patients undergoing CEA, with the commonest failures being in documentation, public health awareness and the environment delivering care. These factors should be optimised to improve the quality of care delivered to high-risk patients undergoing CEA.

Introduction

This chapter will use qualitative methodology to identify points of harm in the CEA pathway of symptomatic patients. This will build on previous chapters that described the scale of iatrogenic harm and the effect of structural factors on CEA and CAS procedural outcomes.

Qualitative Research

Qualitative research includes methodologies that contextualise experiences, behaviours and interactions using descriptive or textual narratives.[1, 2] It allows in-depth analysis of complex issues, without using statistics or quantification.[1] Qualitative research yields rich information relating to experiences and perceptions of health and disease and interactions between patients and healthcare services.[1] This is relevant to this study. Qualitative methodologies also allow better understanding of problems, which may require further investigation. This is the case in this study, which will form the basis of the HFMEA in the next chapter.

Contrasting Qualitative and Quantitative Research

Quantitative research refutes or confirms hypotheses by transforming observations into numerical data and applying statistical analyses, before making generalisations.[3] This 'empirico-analytical' paradigm relies on objectivity and neutrality and is unable to provide insights into subjective experiences or the effect of context or culture on processes.[1] Qualitative methodology aims to understand human actions and experiences by focussing on individuals' views. Both methodologies require sound study design, rigorous data collection and balanced reporting of findings for validity.[1]

Quantitative research also has a fixed research question. This does not change and the methodology is designed to address that objective. However, in qualitative research, broad questions identify the focus of the inquiry before being refined. This iterative or 'emergent' process means that the initial research question may change depending on preliminary data.[1]

A final difference between these methods is that sample size is integral to quantitative research validity as it determines the representativeness of the sample to the population and generalisability of findings. However, in qualitative research, fewer participants may be recruited so long as sufficient depth of information has been gathered to describe the process under investigation (hours of observations or interviews may be large). This continues until themes are developed, patterns are recurring and further sampling is unlikely to provide substantially more information, referred to as 'saturation'.[1]

Various techniques can be used for data collection in qualitative research.

Qualitative Techniques

Interviews are suited to phenomenological research that describes phenomena such as events, situations or experiences.[1] Interviews are powerful in understanding participants' views in the context of experiences. They may be unstructured (participant-led) or semi-structured (focused on a topic).[1] Interviews can be tailored to individuals or groups and can explore deeper meanings whilst allowing participants to contribute relevant material. This makes them suited to 'grounded theory' research where researchers do not have a pre-determined hypothesis with theories 'grounded' in the data collected and developing as data are analysed.[1] This may require alterations to interview questions. However, interviews are time-intensive, with a large amount of material requiring analysis. Facilitation and recording of interviews is also required.

Focus groups consist of individuals that have a shared concern relevant to the study. Facilitated discussion allows the research topic to be explored with group interaction adding to the richness of the material gained.[1] Various views may be represented with the collective view of the group also understood. Such 'action research' focusses on finding solutions to problems and empowers practitioners to drive change.[1] HFMEA is an example of action research that will be detailed in Chapter 4. Limitations of focus groups include difficulties facilitating large groups, lack of participation and/or resolving conflicts arising from differing viewpoints. Also, minority positions may be overlooked if the majority of the group have a different perspective.

Ethnography allows studying of teams or organisations in their practising environment to understand interactions and behaviours.[4] By immersing themselves within the subjects' environment, the observer gains a rich, in-depth knowledge about the nature of the working environment and its effect on processes. Due to the complexity of interactions and behaviours that are observed and recorded, the observer takes field notes. These include the layout of the working environment, the people contributing, activities that are occurring, sequence of events, aim(s) of activities and emotions/thoughts that are expressed.[4] These observations also include review of documents (such as case notes), especially when the observer is absent from the location.[4] Common themes are identified from observations, allowing inferences regarding observed processes. Ethnography yields a rich understanding of how a system works in its natural environment, including observation of subtleties that may otherwise be missed.[4] Supplementation of observations with interviews also provides more candid accounts than if they occurred more formally.[4] However, gaining approval for observations and collecting data is time-intensive, with the clinical environment being unpredictable.[4] Comprehensively recording all aspects of a process is also difficult whilst the observer may be regarded suspiciously and behaviours may change to avoid negative points being observed (the Hawthorne effect).[4]

Rationale for Study

Observation of the carotid surgical pathway in symptomatic patients has never been performed. By using non-participant ethnography (supplemented by semi-structured interviews), areas where harm (or potential harm) occurs may be identified. Reasons for inherent variation in the pathway may also be better understood. Results from such a study may provide insights into improving the quality of care delivered from the perspective of patients and healthcare professionals.

Aim

This study aimed to identify, for the first time, where harm or potential harm may occur to symptomatic patients during their care pathway, from initially experiencing their neurological event until discharge following CEA.

Methods

The methodology used in this study is similar to related studies[5-8] and involved observations during (8am-5pm) and outside working hours (5pm-8am), over a 6-week period, on weekdays (including a Public Holiday) and weekends.

Stroke and Vascular Services

Gloucestershire Hospitals NHS Foundation Trust is one of the largest Trusts in the country, serving more than 612,000 patients.[9] The Trust accommodated more than 250,000 referrals and almost 500,000 first outpatient appointments in 2016-2017.[9] There were also 158,704 inpatient admissions and 134,077 emergency cases.[9] The Trust's 908 beds are divided between 2 District General Hospitals – Cheltenham General Hospital and Gloucestershire Royal Hospital.[9]

Cheltenham General Hospital provides services including General Medicine, General Surgery, Vascular Surgery and Critical Care (with a 24-hour ED). Gloucestershire Royal Hospital has a Trauma Unit and provides access to specialties including Orthopaedic Surgery, Maternity, Paediatrics and Stroke Medicine (with a 24-hour ED).

The Vascular Surgery Department is the hub of the Vascular Network, receiving referrals from Gloucestershire Royal Hospital and Great Western Hospital (Swindon). All major elective and emergency vascular operations are carried out at Cheltenham General Hospital.

The team consists of 7 Consultants, supported by Junior Doctors (who cover patients admitted on the vascular ward). A Vascular Consultant is on-call 24 hours a day at Cheltenham General Hospital with 24-hour access to Vascular Operating Theatres and Critical Care.

Observations were conducted in TIA clinics (in Gloucestershire Royal Hospital and Great Western Hospital), on the Hyper-Acute Stroke Unit (HASU) at Gloucestershire Royal Hospital, in Vascular Surgery Outpatient Clinics (in Gloucestershire Royal Hospital and Cheltenham General Hospital) and on the vascular ward in Cheltenham General Hospital. The observer was external to the organisation where the study took place and unknown to staff.

Inclusion/Exclusion Criteria

Consecutive patients (over 16 years old) presenting with strokes, TIAs or amaurosis fugax between May – July 2019 were observed from initial contact with Stroke Physicians (in TIA clinic or on HASU). Patients presenting with non-ischaemic strokes or pathology unrelated to carotid artery stenosis were excluded as were patients unsuitable for CEA. Patients discharged directly from ED with no follow-up were also excluded and no patients were pre-selected.

Validation and Ethics

Before the study commenced, the observer (KG) was trained in principles of ethnographic methodology and recording accurate, contemporaneous field notes by PC. The study's nature as a quality improvement project (QIP) meant that formal ethics approval was not required. However, the study was approved as a QIP by Gloucestershire Research Support Service and registered with Gloucestershire Hospitals NHS Foundation Trust (Appendix II; registration number: SG190408). The study was also approved as a QIP by the Quality Improvement Lead and Research and Innovation Department at Great Western Hospital and permission was obtained from Stroke Physicians working in Gloucestershire Royal Hospital and Great Western Hospital and Vascular Surgeons working in Cheltenham General Hospital.

Observations

The observer was present at the first clinical encounter with the Stroke Consultant. Once a diagnosis of ischaemic stroke secondary to carotid artery stenosis (>50% NASCET method) was established, the observer sought verbal consent from the patient for participation in this study. The patient was made fully aware that their care would be observed as part of a QIP and the observer would not participate in managing their condition (Appendix III).

Once informed consent was obtained, the time from the patient experiencing symptoms to being reviewed by a Stroke Consultant was retrospectively assessed via a short semi-structured interview (Appendix IV). Thereafter, observations were prospective and in real-time. Field notes were taken assessing: clinical assessment(s); investigations; management; communication; documentation; medications/prescribing; timing; environment; staffing; MDT participation; and infection control. These factors have been assessed in observational studies of General Surgery patients.[5, 6] Data were anonymised at the point of collection.

The entire patient journey was observed (directly and indirectly). Direct observations took place in ED, HASU, Stroke Rehabilitation ward, TIA clinic, Vascular Surgery ward and Vascular Surgery Outpatient Departments. Observations ceased when the patient was discharged from hospital following CEA. For patients discharged pending CEA, short telephone interviews were conducted to ensure no harm had occurred whilst waiting for surgery and observations resumed from the day of admission until discharge following CEA. Patients were contacted by telephone at day 30 post-CEA to detect any complications since discharge.

A pre-prepared *pro forma* (ratified by PC) was used to record observations in all locations to minimise bias (Appendix V). Short interviews with Medical and Nursing staff involved in the patient's care were conducted to supplement observations (Appendix VI) and field notes were also supplemented by case note review. This 'triangulation' is a well-recognised technique.[4]

Data Analysis

Observations from the first three patients were discussed with PC to ensure relevant and timely information was recorded and the study protocol was being followed. Once PC was satisfied, observations of the remaining patients continued.

Field notes were reviewed and common themes identified iteratively, allowing identification of points of harm caused by structural failures.

Study Outcomes

The primary outcome was the number of adverse events. This was defined as any unintended injury that occurred to the patient (including related to medical management).

Secondary outcomes were the number of serious incidents and non-critical events. Serious incidents were defined as events with the potential to cause harm to the patient (including iatrogenic causes) and non-critical episodes were incidents that were inconveniencing from a patient's perspective (medical management may have been optimal).

Delays in patients contacting medical services following symptoms, time-to-review by a Stroke Consultant and Vascular Consultant and days from vascular review to CEA were also quantified.

Results

Ten patients were observed for 1,072 hours over 6 weeks.

Demographics (Table 3.1)

Median age was 79.5 (range: 56-87) years and 70% were male. There were 3 never smokers, 2 current smokers and 5 ex-smokers.

Five patients (50%) presented with strokes, three (30%) had TIAs and two (20%) experienced amaurosis fugax. All stroke patients and one TIA patient were admitted. The remaining TIA patients and those with amaurosis fugax were treated as outpatients.

Surgical Outcomes (Table 3.2)

There were no deaths, strokes or MIs in the nine patients who underwent CEA. Three (33%) patients had post-operative hypotension which settled within 24 hours and one (11%) patient received oral antibiotics for a post-operative chest infection. There were no 30-day complications following discharge after successful CEA.

Median delay from symptoms to surgery was 7.5 (range: 5-40) days. Seven (70%) patients had CEA scheduled within 14 days of symptoms whilst five (50%) patients had CEA scheduled within 7 days of symptoms.

Study Outcomes (Table 3.3)

There were 110 patient safety incidents where harm or potential harm may have occurred – a rate of one incident approximately every 10 hours. In total, 10 (9.1%) were adverse events, 66 (60.0%) were serious incidents and 34 (30.9%) were non-critical events. Half of patients experienced an adverse event between their symptoms and discharge post-CEA.

These incidents are described below, based on the structural factor(s) causing the failure(s).

Table 3.1: Demographic details, comorbidities, presenting symptoms and degree of carotid artery stenosis of all patients observed.

Patient	Age (years)	Sex	Comorbidities	Smoking status	Presenting symptoms	Percentage Stenosis	Inpatient/ Outpatient
1	78	Male	Aortic valve replacement Hypertension BPH	Ex-smoker	Right-sided Amaurosis Fugax	70-79%	Outpatient
2	82	Male	Bilateral hygromas Prostate Cancer – treated Glaucoma	Never	Right-sided Amaurosis Fugax	50-59%	Outpatient
3	80	Male	MI – stents x2 Hypertension Carpal Tunnel syndrome	Ex-smoker	Expressive dysphasia and right-sided weakness (TIA)	60-69%	Outpatient
4	84	Female	Hypertension Psoriasis AF COPD	Ex-smoker	Dysphasia (TIA)	50-59%	Outpatient
5	74	Male	Hypertension Osteoarthritis CKD	Ex-smoker	Left-sided weakness (stroke)	~50%	Inpatient
6	75	Male	Glaucoma COPD CKD	Current	Left-sided weakness and facial droop (stroke)	>90%	Inpatient
7	79	Female	TIA AF Cataract	Never	Right arm weakness (TIA)	60-69%	Inpatient
8	56	Male	LV dysfunction MI – stent x1 T2DM	Current	Left-sided paraesthesia (stroke)	>90%	Inpatient
9	82	Male	Hypertension Hypercholesterolaemia	Ex-smoker	Left-sided weakness (stroke)	60-69%	Inpatient
10	87	Female	Hypertension Hypothyroidism	Never	Right-sided weakness (stroke)	>90%	Inpatient

Abbreviations – AF: Atrial Fibrillation; BPH: Benign Prostatic Hyperplasia; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmunory Disease; LV: Left Ventricular; MI: Myocardial Infarction; T2DM: Type 2 Diabetes Mellitus; TIA: Transient Ischaemic Attack.

Table 3.2: Surgical outcomes and timing across the patient pathway, between index event and CEA, for all included patients.

Patient	Symptoms to Stroke Team review (days)	Symptoms to Vascular Referral (days)	Vascular referral to review (days)	Vascular review to surgery (days)	Surgery to discharge (days)	Symptoms to Surgery (days)	Post-surgical Complications
1	2	2	1	2	1	5	Nil
2	3	3	1	2	2	6	Nil
3	3	3	1	1	2	5	Nil
4	11	11	3	11	N/A	25	N/A
5	3	3	2	17	3	22	Hypotension
6	1	2	3	1	1	6	Nil
7	1	2	1	2	4	5	Nil
8	6	8	1	5	3	14	Hypotension
9	0	2	1	37	2	40	Hypotension
10	1	5	3	1	4	9	Chest infection

N.B. Patient 4 had their CEA cancelled on the day of surgery and were subsequently treated medically.

Table 3.3: Numbers and examples of adverse events, serious incidents and non-critical events identified in the study, based on the structural factor(s) that contributed to the failure.

Structural Factor	Adverse Event	Serious Incident	Non-Critical Event	TOTAL
Public Health	n=3 e.g. recurrent symptoms due to delay in patient presentation	n=14 e.g. patients not recognising symptoms as stroke/TIA		**17**
Clinical Assessment		n=5 e.g. patient not reviewed daily on ward round		**5**
Clinical Management	n=3 e.g. post-CEA hypotension due to prolonged NBM time	n=3 e.g. failure to act on Carotid Doppler result over weekend		**6**
Communication		n=2 e.g. no TIA clinic referral received for a patient from ED	n=6 e.g. patients not consented for CEA by Vascular Consultant	**8**
Documentation		n=20 e.g. no post-operative instructions written		**20**
Prescribing	n=2 e.g. sub-therapeutic rivaroxaban in an AF patient who had a TIA		n=9 e.g. delay in leaving hospital due to waiting for medications	**11**
Timing	n=1 e.g. delay in CEA leading to recurrent symptoms	n=6 e.g. CEA scheduled beyond 14 day national target	n=3 e.g. delay in CEA on day of surgery due to emergency case	**10**
Environment		n=3 e.g. patient presented to a hospital without HASU on site	n=13 e.g. noisy wards and bed moves in the middle of the night	**16**
Staffing		n=3 e.g. CEA cancelled on the day due to lack of staff	n=3 e.g. multiple Vascular Consultants involved in care	**6**
Infection Control	n=1 e.g. post-operative hospital-acquired chest infection	n=10 e.g. omissions in hand washing between reviewing patients		**11**
TOTAL	**10**	**66**	**34**	**110**

Abbreviations – AF: Atrial Fibrillation; CEA: Carotid Endarterectomy; ED: Emergency Department; HASU: Hyper-Acute Stroke Unit; NBM: Nil By Mouth; TIA: Transient Ischaemic Attack.

Adverse Events

Public Health

Three patients delayed presentation to medical services, leading to recurrent neurological episodes. One patient who experienced amaurosis fugax "thought it was cataracts" and ignored his symptoms for months whilst another experienced transient left-sided weakness and paraesthesia but "thought it was shoulder arthritis playing up". The latter patient presented to ED when his speech became slurred and his neighbour suggested he was having a stroke. The third patient ignored his left-sided weakness and transient visual disturbance for 3 days before his wife "insisted to get checked out".

Clinical Management/Timing

One patient was reviewed by a Vascular Consultant and discussed at the MDT meeting, which suggested a CT angiogram. Whilst waiting for this scan, he presented to ED with recurrent symptoms (dysphasia). Imaging was completed and his CEA expedited.

Four patients were kept 'nil by mouth' (NBM) greater than 24 hours peri-operatively. Of these, two experienced post-operative hypotension. One patient was admitted to HDU whilst the other spent the night in Recovery due to lack of HDU availability. Their LOS was prolonged by 1 day.

One patient had their CEA cancelled on the day of surgery due to high blood pressure, despite receiving pre-operative assessment. This patient did not have their CEA rescheduled and was managed medically. They had experienced neurological symptoms 25 days previously so further delay in CEA was thought to place the patient at greater risk of harm than benefit.

Prescribing

One patient was reviewed by a Stroke Consultant and diagnosed with a TIA. However, her rivaroxaban dose was identified as being sub-therapeutic for primary prevention of thrombo-embolic stroke due to atrial fibrillation.

One patient had post-operative hypotension, requiring HDU admission, possibly due to ingesting lisinopril on the day of surgery. Their LOS was prolonged by 1 day.

Infection Control

One patient developed a post-operative hospital-acquired chest infection. This was treated with oral antibiotics and prolonged their LOS by 2 days.

Serious Incidents

Public Health

No patients (0%) realised they were having a stroke/TIA when they experienced neurological symptoms. One patient's sister, two patients' sons, two patients' friends and one patient's wife recognised the symptoms and called an ambulance or drove them to ED. Three patients delayed presentation to medical services, causing recurrent episodes (previously discussed) whilst one patient mentioned her symptoms to her General Practitioner (GP) in an appointment for an unrelated problem 6 days later which resulted in TIA clinic referral.

Environment

Two patients presented to Cheltenham General Hospital with TIA symptoms when they should have attended Gloucestershire Royal Hospital as it has a HASU on-site (not present in Cheltenham General Hospital). One patient was reviewed by Ophthalmology and referred to TIA clinic with suspected amaurosis fugax whilst the other was admitted and transferred to Gloucestershire Royal Hospital HASU.

One patient suffered from post-operative hypotension, requiring metaraminol. HDU admission was not possible due to lack of beds so they spent the night in Recovery.

Staffing

Two patients experienced neurological events over the weekend. One drove to ED for assessment as "the GP Practice was closed". The other waited until Tuesday for the GP Practice to open (after a Public Holiday) before trying to make an appointment. When they "couldn't get an appointment", they "waited until 5pm for the Duty Doctor to call back". When "the call never came", the patient's wife took him to ED.

One patient had their CEA cancelled on the day of surgery due to "staffing issues". They were told by the Vascular Consultant that they "couldn't do the surgery" as they had "ran out of time due to over-running cases and emergencies". However, the Vascular Consultant rescheduled the operation and performed CEA the next morning.

Timing

Two patients were delayed being reviewed in TIA clinic after the referral was received by the Clinic Coordinator. One was seen 3 days after being referred as they were deemed low-risk following triage of the referral by the Stroke Consultant. The other was referred on the Thursday before a Public Holiday. As there was no space on Friday and TIA clinic was closed over the weekend and Public Holiday, the patient was not reviewed by a Stroke Consultant until Tuesday (5 days following referral).

One patient had a delay in undergoing CEA as they were reviewed by the Vascular Consultant on a Friday and told "this operation doesn't happen over the weekend". They were also "feeling overwhelmed" after being presented the risks and benefits of surgery and were reluctant to proceed as this Consultant's on-call week was finishing. The Consultant told them to "think about it over the weekend", after which they phoned his secretary on Monday to confirm their intention to proceed with surgery.

One patient's Vascular Consultant review was delayed as the referral was made by the Stroke Consultant on a Saturday. As the Vascular Coordinator did not work on weekends, the Stroke Consultant directly spoke with the Vascular Consultant on Monday and arranged for the patient to be transferred to Cheltenham General Hospital that same day for vascular review and surgery. No contact between the Stroke Consultant and Vascular Consultant over the weekend introduced a delay.

Two patients underwent CEA beyond the national target of 14 days from symptoms to surgery. This was following MDT discussion and recommendation for further imaging in one case and an "interval CEA" in another case "to let the brain recover". The first patient had recurrent neurological symptoms whilst waiting for his CEA (previously discussed) but the other patient did not come to harm.

Documentation

No notes were available for the Stroke Consultant to review when assessing three patients in TIA clinic. This was also the case when the same patients were reviewed by the Vascular Consultant the next day.

One patient had no post-operative instructions written by the Consultant and the Medical team were unsure how to manage them once transferred back to the vascular ward. This patient also recounted that "the Consultant came and saw me in Recovery" but this was not documented.

Two further patients had documentation omissions following Vascular Consultant review. In one case, the Vascular Consultant reviewed them following referral by the Stroke Consultant. He decided to discuss the patient in the MDT meeting that same afternoon. However, the MDT discussion and outcome were not documented. Another patient was reviewed by the Vascular Consultant on the ward round prior to surgery. However, this was also not documented.

There were documentation errors in the notes of all patients. This consisted of either an incorrect date or an omitted time of the ward round which did not result in patient harm.

Communication

One patient was referred to TIA clinic following ED review. The patient and their wife were advised they would be "called to have a scan and seen in clinic within the next few days". When "there was no contact" after 2 days, the patient's wife "called up the TIA Clinic Coordinator to chase up the appointment" as she was "worried". The TIA Clinic Coordinator advised that she had not received the ED referral but arranged for the patient to be seen that same day.

There was also miscommunication regarding one patient's CEA date. When leaving their pre-operative assessment, they were advised a date for surgery (18 June) and where to present. However, a few hours later, a Secretary called and gave a different date for CEA (21 June). On 14 June, the patient received a call at 8:45am from the hospital asking where they were as they were expected for surgery. The Vascular Consultant also called the patient at 9:30am and, as they had not eaten breakfast, "he requested that I come in immediately for an operation". The patient commented that "they should have been more specific to avoid the mix up in communication" but "having the operation done was the most important thing".

Clinical Assessment/Management

One patient's referral to Vascular Surgery was delayed by the Stroke team as their Carotid Doppler was performed on a Friday and the result was not reviewed until Monday. This patient was not reviewed over the weekend on HASU. Once the result had been reviewed, they were referred the same day. This delayed this patient's vascular review and CEA.

One patient spent 18 days on the Stroke Rehabilitation ward and was deemed "medically fit for discharge" for 7 (38.9%) of those days. They were reviewed on alternate days by members of the Medical team and 5 times by the Stroke Consultant during their hospital stay. No ward rounds occurred on weekends or Public Holidays on the Stroke Rehabilitation ward. They required input by Occupational Therapy but their LOS may have been prolonged by a lack of regular Medical input. This caused the patient frustration and they often stated "this is wasting my time and theirs" and "I'm taking up a bed and not helping anybody". It didn't make sense to the patient "why they can't release me" and there was "no real reason for keeping me here". The patient was confused that "plans keep changing and there is a lack of organisation" and it seemed to them that "there's nothing I couldn't have done at home".

Two patients were not reviewed by the Vascular Consultant on their first post-operative day. Of these patients, one was on the vascular ward but the "Consultant was called away to an emergency". The patient was seen by the Registrar and discharged home, without Consultant input. The second was recovering in HDU due to post-operative hypotension. They were reviewed by the Critical Care team and transferred to the vascular ward later that day. The patient was reviewed by the Vascular Consultant the following day.

Four patients were kept NBM greater than 24 hours peri-operatively. Of these, one waited all day for surgery before it was cancelled and rescheduled for the next day. Another patient was NBM for approximately 36 hours as they were "too drowsy to eat" following CEA so they "didn't eat anything until breakfast the next day", resulting in "feeling very weak". The other 2 patients experienced post-operative hypotension (previously discussed).

Infection Control

All patients were subject to hand washing omissions but no patients developed wound infections or complications due to this infection control failure. One patient commented "not everybody washes their hands between patients, which is a bit worrying".

Non-Critical Events

Environment

Two patients had interruptions whilst being assessed. One was interrupted during TIA clinic review by the Stroke Consultant whilst the other was interrupted during pre-operative assessment. Neither interruption breached patient confidentiality.

Four patients made multiple trips to Gloucestershire Royal Hospital and Cheltenham General Hospital during their treatment. One made 4 separate trips for TIA clinic review (Gloucestershire Royal Hospital), vascular review (Cheltenham General Hospital), pre-operative assessment (Cheltenham General Hospital) and CEA (Cheltenham General Hospital). Another was admitted in Gloucestershire Royal Hospital but made 4 trips to Cheltenham General Hospital for vascular review (twice), pre-operative assessment and CEA. A third patient was reviewed by the Vascular Consultant whilst an inpatient in Gloucestershire Royal Hospital. However, they attended Cheltenham General Hospital twice for pre-operative assessment and CEA. The final patient was reviewed by the Vascular Consultant whilst an inpatient in Gloucestershire Royal Hospital. However, they attended Cheltenham General Hospital thrice for another Vascular Consultant review, pre-operative assessment and CEA. Patients stated it was "no bother going between hospitals" as "it's got to be done".

Three patients were transferred between Gloucestershire Royal Hospital HASU and Cheltenham General Hospital for Vascular Consultant review. Two were transferred to the vascular ward at Cheltenham General Hospital and remained until discharge post-CEA. One patient was transferred from Gloucestershire Royal Hospital HASU to Cheltenham General Hospital for Vascular Consultant review before being transferred back, disrupting lunch.

One patient had a "rough night" on the vascular ward due to repeat blood pressure checks all night. They had been transferred earlier in the day from HDU due to post-operative hypotension but a Nurse took their blood pressure "every 15 minutes, all night".

Three patients identified "noisy wards" and "overnight bed moves" as factors contributing to a negative experience. Whilst they recognised noise levels would be high due to "beeping machines and distressed patients", one patient described the environment as "pretty grim overnight". All three patients were moved beds between 2:00-4:30am, disrupting sleep.

Staffing

Three patients had more than one Vascular Consultant involved in their care. Two were reviewed and discharged over the weekend by a different Vascular Consultant to the one who had performed their CEA. One patient was reviewed by the on-call Vascular Consultant but they were unable to operate on them expeditiously so they arranged for the patient to have their surgery the following week by a different Vascular Consultant.

Timing

Two patients waited 1.5 hours for Vascular Consultant review as he was on-call and "delayed in theatre". Another patient's CEA was delayed by 5 hours as "an emergency came in". The Vascular Consultant "apologised for the delay" which contributed to prolonging his NBM time.

Communication

Six patients were not consented for CEA by the Vascular Consultant. One patient was consented by a Registrar and another by a Core Surgical Trainee who were both experienced in the risks/benefits of the operation. Whilst 'delegated consent' is recognised practice, four patients were consented by Advanced Nurse Practitioners (ANPs) who had "only seen the procedure a few times". ANPs used pre-printed stickers to standardise consent forms.

Prescribing

All discharges were "delayed by waiting for tablets". In one case, "the ward ran out of aspirin".

Discussion

This novel ethnographic study that observed the carotid surgical pathway of symptomatic patients for 1,072 hours identified 110 incidents where patients were harmed or at risk of harm – a rate of one incident approximately every 10 hours. Almost 10% were adverse events, with half of patients experiencing adverse events from their symptoms until discharge following CEA. Various structural factors were responsible for these incidents, the commonest failures being in documentation, public health awareness and the environment delivering care. These findings have identified targets for improvement in the quality of care delivered to high-risk patients undergoing CEA.

Contextualising our Results

Our findings are consistent with other studies that quantified the extent of iatrogenic harm. In the UK, Vincent *et al*.[10] reported an adverse event rate of 10.8% in 1,014 patients whilst Sari *et al*.[11] found that 8.7% of 1,006 admissions suffered an adverse event. Similar studies in Denmark[12], New Zealand[13], Canada[14] and Sweden[15] also demonstrated similar incidences of adverse events. A systematic review of 16,424 surgical patients reported an adverse event rate of 11.6%, with the commonest causes related to monitoring, incomplete or delayed treatment and diagnostic error or delay.[16] A more recent meta-analysis of 337,025 patients reported that preventable patient harm was most prevalent in surgical specialties, at a rate of 10.0%.[17] This was similar to the findings of another systematic review that performed a retrospective, cross-sectional analysis of the Nationwide Inpatient Sample (NIS) in the USA and reported an adverse event rate of 12.9% in 2,508,917 patients following major cancer surgery.[18] These authors reported a significant association between experiencing adverse events and increased

in-hospital mortality, LOS and hospital charges (all $p<0.001$).[18] Our finding that 9.1% of all incidents were adverse events is comparable to these studies and a systematic review of 74,485 patients that examined adverse events in inpatients and outpatients.[19]

However, we also found that half our patients experienced adverse events. This is higher than previous studies and is likely to be multi-factorial. Previous studies reviewed case notes to identify adverse events which may have under-estimated the true incidence of adverse events as subtle incidents may have been missed due to documentation inaccuracies. Our patients may have been higher risk than in previous studies as they had significant comorbidities (Table 3.1) and surgery is associated with a higher incidence of adverse events.[19-21] The CEA pathway is also complex with inpatient and outpatient interactions between healthcare professionals and relies on patients seeking medical attention after experiencing their neurological event. This may have increased the incidence of adverse events. Moreover, this study's comprehensiveness (following inpatients and outpatients throughout their care pathway) means that more incidents may be detected compared to previous studies that examined a section of the pathway. Our sample size of 10 patients may have also exaggerated the adverse event rate.[22]

Themes in Errors

Several structural factors interact to cause errors. One patient had post-operative hypotension possibly due to taking lisinopril on the day of surgery. This required HDU admission and prolonged their LOS. The failures in this patient's care included: clinical assessment; management; communication; documentation; and prescribing. If this problem had been identified at pre-operative assessment (clinical assessment), a management plan could have been prepared (management), documented (documentation) and communicated (communication) with the patient to omit lisinopril on the morning of CEA. This may have

avoided this issue, preventing HDU admission and reducing LOS. This is an example of the Swiss cheese model (where errors in several domains align to cause an adverse event).

Patients also experienced several failings due to different structural factors throughout their pathway. One patient did not recognise their symptoms as a TIA (public health failing) and mentioned it to their GP during a consultation for an unrelated condition. There was a delay in scheduling their TIA clinic appointment (timing failure) due to the GP referral arriving with the TIA Clinic Coordinator on Friday afternoon. When seen by the Stroke Consultant, he identified the patient's rivaroxaban dose was sub-therapeutic for primary prevention of thrombo-embolic stroke due to atrial fibrillation (failure of prescribing and management). Later in the pathway, the patient felt "overwhelmed" and "bombarded with information" during the discussion regarding risks and benefits of CEA with the Vascular Consultant (failure of communication) so they were advised to "think about it over the weekend". Once they decided to proceed, they attended pre-operative assessment on a separate day to CEA and there were also several interruptions during this consultation (failure of environment). The patient's CEA was cancelled on the day of surgery due to high blood pressure. However, there had been opportunities to correct this prior to the operation (failure of clinical assessment and management). There had also been failures of documentation and infection control during this patient's care. Such a case highlights the multiple domains of a patient's care pathway that require optimisation to prevent errors, as suggested by the World Health Organisation (WHO) in their *Third Global Patient Safety Challenge* report.[23]

Common Errors

The commonest causes of incidents were documentation errors, lack of awareness in recognising stroke symptoms, failings in the environment and infection control lapses.

Documentation errors were present in the notes of all patients. These could be trivial omissions (e.g. time of entry or incorrect date) or potentially serious (e.g. no post-operative instructions). In the digital era, a paperless system with electronic patient notes should be ubiquitous. This may eliminate many documentation errors observed in our study and save time locating patient notes. Communication may also be enhanced as referrals from other specialties would be less likely to be lost (one patient's case) whilst misunderstandings from handwriting that is difficult to decipher may also be eliminated, reducing medical errors. A systematic review reported that electronic patient records significantly reduced documentation time ($p<0.007$) and medication errors ($p<0.001$).[24] However, an appropriate implementation strategy is necessary[24] as suggested by WHO guidelines.[25] Investment would also be required. Therefore, by harnessing the power of technology in healthcare processes, quality of care can be improved.

None of our patients recognised that they were having a stroke, TIA or amaurosis fugax, with 3 patients having recurrent episodes before contacting medical services. This is a failure of public health and patient education. Various studies have investigated reasons for patient delay in presenting to ED after experiencing strokes. Rossnagel *et al*.[26] reported that if patients considered their symptoms as urgent, this decreased delay to ED arrival whereas misinterpreting them as "faintness/weakness" prolonged the time to seeking medical help. This was supported by Mellor *et al*.[27] who reported that patients who perceived their symptoms as serious called an ambulance or went to ED. This is consistent with our study's findings. Various studies have also reported that the proportion of patients arriving at ED within 3 hours of symptoms ranges from 8-58%.[28-33] This is similar to our study where 50% of patients arrived at ED within 3 hours of symptoms. Facial droop and dysphasia have been associated with expedited ED arrival with dysphasia associated with patients calling an ambulance.[31, 33, 34] In our study, 3 patients suffered from dysphasia which may explain the lack of recognition of symptom severity. However, public knowledge regarding stroke is inadequate, with 38%

recognising stroke symptoms and 25% identifying their own symptoms.[35] In the UK, a systematic review reported that patients recognised unilateral weakness and speech disturbance as stroke symptoms but less than half identified themselves having a stroke.[36] Moloczij *et al*.[37] suggested that lack of pain may contribute to patients not recognising stroke symptom severity. However, bystanders recognise stroke symptoms more often than patients, who prefer 'watchful waiting' instead.[27, 33, 38, 39] This supports our findings.

This study has highlighted an opportunity to improve patients' recognition of stroke symptoms so they present earlier to ED. In the UK, the Face Arm Speech Time to call 999 (FAST) media campaign is simple, easy to understand and identifies 88.9% of patients with strokes or TIAs.[40] However, it does not include amaurosis fugax (20% of our patients). Such campaigns increase knowledge about stroke symptoms and the need to present early to ED.[41] However, this increased awareness was not sustained after the campaign ceased in Canada.[41] A German multimedia campaign (in newspapers, television, radio, leaflets and advertisements) also failed to change care-seeking behaviour (despite improving knowledge) with similar proportions of patients calling an ambulance after suffering stroke symptoms before and after the campaign.[42] Whilst these media campaigns can be expensive, it is important to improve public awareness of stroke symptoms and the need to present early to ED. The need to present to an ED with attached HASU is also important as our study found that 40% of patients who self-presented to ED arrived at a hospital with no HASU and required transfer after initial assessment.

Failures in the environment providing patient care also contributed to errors. The VSGBI and GIRFT reports suggested centralisation of Vascular Surgery services, following a hub and spoke model of vascular care in the UK.[43, 44] However, in Gloucestershire, the HASU and vascular ward are in different locations, meaning patients often travelled several times for TIA clinic review, vascular review, pre-operative assessment and CEA. The hub (Cheltenham General Hospital) should have an on-site HASU so vascular review can be streamlined,

requiring restructuring of services. Alternatively, Vascular Consultants could have designated slots in their Gloucestershire Royal Hospital clinics to review stroke patients and decide their suitability for CEA or review them on the HASU. However, this would mean that the on-call Vascular Consultant would not be deciding who would be having surgery but would be responsible for such patients. In our study, 3 patients were operated on by a Consultant other than the on-call Vascular Surgeon, without deficiencies in care. Two (67%) were discharged by a Consultant other than the Operating Surgeon over the weekend. The GIRFT report suggested that scheduled operating should occur at weekends in the hub as most vascular operations should be re-classified as 'urgent' (including CEA).[44] This may reduce handing over of patients between Consultants at the weekend, improving quality of care. This will require investment in the workforce with each hub recommended to have at least 6 Consultants.[43, 44] Cheltenham General Hospital's Vascular Department had 7 Consultants providing 24-hour Consultant-led care, with a vascular ward, Operating Theatre, on-site vascular laboratory, 24-hour access to Critical Care and weekly MDT meetings (all VSGBI recommendations).[43] This minimised failings in clinical assessment and patient management.

Hand washing was frequently omitted following Medical reviews. This is supported by findings in the literature[45] and may be due to heavy workloads.[46] Self-protection, adequacy of supplies and organisational culture influence hand hygiene behaviours.[46] Various studies[46-48] have demonstrated that repeated education in hand hygiene practices, auditing, feedback and easy access to sinks or alcohol gel raise compliance with hand washing between patients and this multi-modal approach is endorsed by the WHO.[49] A systematic review suggested that improvements in patient hand hygiene may improve healthcare worker compliance with infection control practices.[50] Another study reported that hand hygiene practices of seniors and team leaders influence juniors.[51] Therefore, targeting Consultants may improve hand hygiene practices. However, no modality ensures 100% compliance, necessitating further research.

Timing

As previously discussed, in patients with 50-99% carotid artery stenosis, benefit from CEA decreased substantially if delayed more than two weeks after initial neurological symptoms.[52] The number needed to treat (NNT) to prevent one ipsilateral stroke at five years in patients with 50-99% carotid artery stenosis increased from 5 (when CEA was performed within two weeks of neurological symptoms) to 125 (when CEA was performed 12 weeks after symptoms).[52] UK[53], European[54] and North American[55] guidelines recommend CEA is performed within 2 weeks of neurological symptoms whilst the GIRFT report suggested reducing this to 7 days.[44] Timing for CEA is a useful benchmark for the quality of care provided by a vascular unit.

In our study, 70% of patients had CEA scheduled within 14 days of symptoms and 50% within 7 days. Median delay from symptoms to surgery was 7.5 (range: 5-40) days. This compares favourably to the literature. A study performed in the Cheltenham General Hospital vascular unit by Kulkarni *et al*.[56] 10 years previously reported median delays of 97 days between initial event and CEA, resulting in 29% experiencing recurrent cerebral events. There has been a substantial temporal improvement, especially in delays relating to investigation and scheduling CEA (Table 3.2). Another UK study reported temporal improvements in the proportion of patients undergoing CEA within 2 weeks of symptoms from 25% to 40.2%.[57] Median delays improved from 25 to 17 days.[57] This is substantially worse than our results but delays in patient presentation were the commonest reason for delay in CEA, similar to our findings.[57] Other studies have also reported worse results compared to ours. A Scottish study[58] reported median delays between 30-42 days from symptoms to surgery whilst the GALA trial[59] reported median delays of 82 days. Fairhead *et al*.[60] reported delays of 100 days between symptoms and CEA in Oxfordshire whilst Khashram *et al*.[61] reported delays of up to 115 days in New Zealand (with

20-23% operated within 2 weeks of symptoms). The latter study identified patient delay as the primary reason, in keeping with our findings. A Swedish study reported delays from symptoms to surgery of 36 days for local patients and 64 days for regional patients[62] whilst a Finnish study reported improvements in delay from symptoms to surgery from 47 days (11% had CEA within 2 weeks) to 19 days (37% had CEA within 2 weeks).[63, 64] The latter authors identified the main reason for delays was between vascular review and scheduling CEA and reported improvements in performance after increasing capacity on their operating lists and centralising vascular services.[63, 64] Addition of TIA clinics also helped to reduce delays.[64] This is similar to Salem *et al.*[65] who observed 78% of patients underwent CEA within 2 weeks (median 9 day delay from symptoms to surgery) and 44% underwent CEA within 7 days of the index event following establishment of rapid access TIA clinics in Leicester. These results are similar to ours and likely due to similarities in the structure of services provided to symptomatic patients with carotid stenoses in Leicestershire and Gloucestershire (daily TIA clinic; triaging of referrals; rapid access to imaging; early Vascular Surgeon involvement; and transfer for CEA). Overall, it seems that performance monitoring of Vascular Surgeons (via NVR reporting in the UK) and service reconfigurations have helped reduce delays from symptoms to CEA over time.

However, further improvements are required in CEA provision internationally. A Canadian study reported median delays between symptoms and surgery of 25 days (39% had CEA within 2 weeks), with 25% of patients presenting to medical services 2 weeks or more after their index event.[66] This is similar to Meyer *et al.*[67] who reported median delays of 28.5 days from symptoms to CEA also in Canada (30.6% having their CEA within 2 weeks of their index event), with 14.2% failing to access healthcare services within 14 days of initial event. Jetty *et al.*[68] reported an 8% adherence to the 2-week target whilst Andgren *et al.*[69] found that 21% of their cohort underwent CEA within 2 weeks of symptoms (median delay of 26 days). Dutch authors reported a reduction in the delay from symptoms to CEA from 53 (10.5% treated in 2

weeks) to 21 days (32.4% treated in 2 weeks) over 5 years with the introduction of flexible operating schedules and slots to review patients within 48 hours of referral.[70] They recommended classifying CEA as a semi-emergency procedure (similar to the GIRFT report) and also focussing on the pre-hospital phase to minimise delays in patients seeking medical help following their index event.[70] Re-classifying CEA as urgent reduced median times from symptoms to surgery from 83 to 32 days in New Zealand.[71]

Registry studies have also shown improvements over time. A Danish Vascular Registry analysis demonstrated reductions in the median time from symptoms to CEA from 31 to 16 days (increase from 13% to 47% undergoing CEA within 2 weeks of symptoms), despite a 30% increase in the number of CEAs performed.[72] This was achieved by expediting Carotid Duplex Ultrasound scans, dedicating more operating time to CEA and re-classifying CEA as an urgent operation. An analysis from the UK NVR also reported reductions in the median times from symptoms to surgery from 22 to 12 days between 2009-2014 (increasing the proportion undergoing CEA within 2 weeks from 37% to 58%)[73] whilst the German Carotid Registry reported similar reductions in median days from symptoms to surgery from 10 to 8 days between 2009-2014.[74] Our results compare favourably with the published literature. The only reasons for substantial (more than 14 days) delay between symptoms and CEA in our study were patient presentation (n=1), patient deciding whether to have CEA (n=1), MDT discussion (n=1) and interval CEA (n=1). The high-quality care reported in this study is likely due to structural factors such as the presence of a rapid access TIA clinic (with triaged referrals), same-day CT brain imaging and Carotid Duplex (with up to 5 allocated slots for each), e-referral to Vascular Surgery, rapid review by the Vascular Consultant and easy access to CEA operating lists. This excellent performance was achieved with no procedural strokes or deaths and only minor post-operative complications (hypotension (n=3) and chest infection (n=1)).

Strengths

This is the first use of ethnography to observe symptomatic patients undergoing CEA throughout their care pathway. Ethnography has previously been used to identify points of harm on surgical wards[5], in the process of escalation of care in unstable General Surgery patients[6] and to design an error capture tool for complex arterial surgery.[7] The period of observation varied from 42-250 hours in these studies. Our study observed for 1,072 hours, which is significantly longer. Our observations also took place in several hospitals (Cheltenham General, Gloucestershire Royal and Great Western Hospitals) and several locations within those hospitals (TIA clinic, HASU, Outpatients, vascular ward, Recovery). This allowed a representative picture to emerge about problems occurring throughout the CEA pathway as patients were followed in all aspects of care, in different environments. This is important as many specialties are involved in the care of symptomatic patients undergoing CEA so the effect of structural factors on CEA requires observation in different locations. Use of triangulation is a particular strength and saturation was also reached, suggesting that our findings are reliable.

Limitations

The limitations of this study include that observations were limited to a small number of patients (n=10). This modest sample size may not be fully representative of practice in Gloucestershire or nationally. However, as our observations were for 1,072 hours and we reached saturation, this suggests that our findings are reliable and generalisable. Observations were also limited to 3 hospitals. However, these hospitals are large, well-resourced and likely to represent current NHS practice.

It may also be possible that some incidents were not observed, particularly during times that the observer was not in the hospital. Therefore, the results may under-estimate the true incident rate. However, observations were supplemented by case note review and interviews with Medical and Nursing staff involved in the patient's care to minimise the number of incidents missed and our findings are consistent with the literature.

Finally, Clinicians being observed may have been affected by the Hawthorne effect.[75] However, there is uncertainty if such an effect exists and, if it does, to what extent it influences results from ethnography as the Hawthorne effect is more pronounced in artificial, experimental environments rather than naturalistic observations.[76] The fact that our observations were conducted in a dynamic environment limits the Hawthorne effect whilst social connections developed during the observational period may further protect against participants altering their behaviour.[76] The large number of incidents observed suggests the Hawthorne effect was minimal in this 6-week study.

Conclusions and Implications

This ethnographic study that observed the CEA pathway of 10 symptomatic patients for 1,072 hours identified 110 incidents where patients were directly harmed or at risk of harm – a rate of one incident approximately every 10 hours. Almost 10% were adverse events, with half of patients experiencing an adverse event from their symptoms until discharge following CEA. The commonest failures were in documentation, public health awareness and the environment delivering care. These findings have identified targets for improvement in the quality of care delivered to high-risk patients undergoing CEA.

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CHAPTER 4: Improving Safety in the Carotid Surgical Pathway: an Healthcare Failure Mode and Effect Analysis

Abstract

Background: Various studies have used healthcare failure mode and effect analysis (HFMEA) to prevent harm in surgical patients. However, the carotid surgical pathway has never been analysed. This study aimed, for the first time, to systematically analyse the CEA pathway for symptomatic patients, using HFMEA, to understand causes for real or potential harm and provide recommendations to improve patient safety.

Methods: Ethnography was used to prospectively observe the CEA pathway of consecutive patients, presenting to 3 hospitals with strokes, TIAs or amaurosis fugax, between May – July 2019. The pathway was summarised into process steps and failure modes were suggested for each step. A multi-disciplinary panel of 13 stakeholders involved in the care of symptomatic patients undergoing CEA risk assessed each failure mode (based on its perceived frequency, severity and detectability), obtaining contributory factors following group discussion. Recommendations to prospectively prevent these failures were suggested.

Results: Ten patients were observed for 1,072 hours and 65 organisational failures were identified in 51 process steps comprising the CEA pathway. Recommendations were suggested in 5 areas: improve patient understanding to recognise stroke symptoms and educate General Practitioners, Emergency Department Physicians and Opticians to recognise subtle neurological symptoms; improve resource allocation allowing centralisation of stroke and vascular services; implement latest technology to improve documentation, streamline care, enhance efficiency and improve patient safety; use protocol-driven, Consultant-led care to standardise practice in a culture of non-hierarchical, multi-disciplinary team working; and

improve communication between healthcare professionals (including effective handovers and inductions) and also with patients.

Conclusions: Systematic identification of contributory factors to failures in the CEA pathway of symptomatic patients using HFMEA has allowed interventions to be suggested to prospectively reduce adverse events. These recommendations should be subject to clinical audit and may allow an optimised CEA pathway to be constructed for symptomatic patients in the future.

Introduction

This chapter will use findings from previous chapters to systematically analyse the CEA pathway. This will identify factors contributing to potential harm in patients and allow recommendations to improve patient safety and surgical outcomes. Various patient safety models exist.

Patient Safety Models

The Systems Engineering Initiative for Patient Safety (SEIPS) model provides a framework for thinking about different aspects of a system, interactions and effects on outcomes.[1] In the SEIPS model, the healthcare provider ('person') performs various tasks, using tools and technologies, in a physical environment, under organisational conditions.[1] These five components (person, tasks, tools and technologies, physical environment and organisational conditions) interact and influence each other, affecting outcomes.[1] This model allows assessment of the quality of care focussing on these five factors, using techniques such as questionnaires/surveys and patient observation.[1] However, the SEIPS model is limited by indirect involvement of patients and MDT members. Quantification of the risk of various factors contributing to harm is also not possible using SEIPS.

Another model used to understand causes of patient harm is the expansion of the Swiss cheese model. Vincent *et al*.[2] described seven factors that may contribute to error, including organisational and management factors, work environment, team factors, task factors and patient characteristics.[2] However, there is no framework for quantifying risk and prioritising implementation of solutions for problems identified.

The 'Haddon model' also allows assessment of patient harm, focussing on the injurious event itself. The event is thought to be related to the mechanism of injury, the injured person and the environment.[3] The environment is further subdivided into physical (e.g. noise), social (e.g. communication) and biological (e.g. patient characteristics) factors.[3] These can then be further categorised into three phases: pre-event, event and post-event. Whilst this complements the pre-operative, operative and post-operative phases of surgical pathways, it is not possible to quantify risk and prioritise targeting the most serious errors.

Failure Mode and Effect Analysis (FMEA), applied to healthcare (HFMEA), may be a more effective model for analysis of the CEA pathway in symptomatic patients.

FMEA: Background

FMEA identifies various ways that a process fails, why it fails, the effects of failure and steps that can be implemented to mitigate against failures. A multi-stage approach predicts potential failures and suggests strategies to minimise their consequences, preventing adverse events occurring. It was first applied to the aerospace industry, before establishing itself as the primary method for risk reduction in the automotive and aviation industries.[4-6]

Early proponents of HFMEA used it to prevent medication errors in hospitals, particularly in complex environments such as ICUs.[7] HFMEA identified ineffective communication between Surgeons and Anaesthetists post-operatively, recommending standardised care pathways, protocols and checklists to improve handovers between healthcare professionals.[8] Analysis of failures to escalate unwell surgical patients using HFMEA also identified factors such as outdated technology, lack of staff and hierarchy as barriers to effective communication.[9] Recommendations included using escalation protocols, human factors education, modern

communication technology and improved clinical supervision to overcome potential causes of patient harm.[9] Using HFMEA to analyse hazards on surgical wards identified inadequate hand hygiene, errors in measuring and responding to vital signs, failure to administer the correct medication and ineffective handover as contributors to increasing risk of patient harm.[10] Recommendations included standardisation of processes, simplification of equipment design, electronic prescribing and automation of vital sign measurement.[10]

HFMEA has also be used in Bariatric surgery to identify inadequate medical management of obese patients, inappropriate equipment use and inability to locate equipment for patient transport as failure points.[11] Recommendations included labelling load-sensitive equipment with weight limits, training staff in Bariatric patient management and procurement of appropriate equipment.[11] HFMEA has also been applied to laparoscopic Colorectal surgical training to acquire non-technical skills.[12]

Rationale for Study

HFMEA allows in-depth, systematic analysis of surgical processes with involvement of patients and MDT members, providing valuable insights from their perspectives, expertise and experience. Patient participation is particularly valuable and this unique characteristic differentiates it from other models of incident analysis. Moreover, it prospectively risk assesses failures rather than relying on retrospective analyses, which may be biased. It also allows quantification of potential errors that may cause harm according to their frequency, severity and detectability, leading to targeting the highest-risk steps in a process, maximising benefit of interventions. HFMEA also allows assessment of an entire pathway whereas other models provide more narrow analyses. HFMEA has never been used to analyse the CEA pathway and may provide insights to prevent harm in high-risk symptomatic patients.

Aim

This study aimed to systematically risk assess the CEA pathway for symptomatic patients, using HFMEA, to identify points of harm, prioritise healthcare process failures, understand their contributory factors and provide recommendations to improve patient safety.

Methods

This study was conducted in 4 stages, using similar methodology to other HFMEA analyses in surgical patients[9, 10], validated by the Veterans Affairs National Center for Patient Safety.[13] Briefly, the first stage involved observation of the carotid intervention pathway to define it and understand reasons for variation in care. The second stage required risk assessment of the pathway by a multi-disciplinary panel of stakeholders involved in the care of symptomatic patients undergoing CEA. The third and fourth stages involved a focus group identifying contributory factors for each failure mode and recommending interventions that may be implemented to prospectively prevent failures occurring.

The study's nature as a QIP meant that formal ethics approval was not required. However, the study was approved as a QIP and registered with Gloucestershire Hospitals NHS Foundation Trust (Appendix II; registration number: SG190408).

Phase One – Observation

Non-participatory ethnographic observations were performed in Gloucestershire Royal Hospital, Cheltenham General Hospital and Great Western Hospital (Swindon) for 6 weeks, between May – July 2019, as described in Chapter 3. The observer was external to the organisation where the study took place and unknown to staff members.

After obtaining verbal consent, consecutive patients (over 16 years old) presenting with strokes, TIAs or amaurosis fugax were prospectively observed from initial contact with Stroke Physicians (in TIA clinic or on HASU) until discharge following CEA. The time from the patient experiencing symptoms to being reviewed by a Stroke Consultant was retrospectively assessed via a short semi-structured interview. Data were anonymised at the point of collection.

Patients presenting with non-ischaemic strokes or pathology unrelated to carotid artery stenosis were excluded as were patients unsuitable for CEA. No patients were pre-selected. Ethnography allowed the observer to define the CEA pathway and understand reasons for variation in patient care. This enabled a flow diagram of the entire pathway to be produced. Process steps were defined and similar activities collated to summarise the CEA pathway. Failure modes for each step were suggested, informed by observations.

Phase Two – Risk Assessment

Failure modes were risk assessed by each member of a multi-disciplinary panel of 13 stakeholders involved in the care of symptomatic patients undergoing CEA to quantify each participant's perceived level of risk associated with each process step.

The focus group included at least one of each of the following:

- Consultant Stroke Physician (n=1)
- Consultant Vascular Surgeon (n=2)
- Consultant ED Physician (n=2)
- Consultant Anaesthetist (n=1)
- GP (n=2)
- Vascular ANP (n=1)
- Stroke Specialist Nurse (n=1)
- Vascular Coordinator (n=1)
- TIA Clinic Coordinator (n=1)
- Patient (n=1)

Participants risk assessed each failure mode based on three 4-point scales quantifying the perceived frequency, severity and detectability of organisational failures in patient care (Table 4.1). Mean scores were multiplied to produce a mean hazard score (maximum score: 64).

Table 4.1: Scoring matrix assessing the risk for each failure mode, based on its frequency, severity and detectability.

Score	Frequency	Severity	Detectability
4	High (1 per day)	Death	Remote
3	Moderate (1 per week)	Any Disability	Low
2	Infrequent (1 per month)	Increased Length of Stay	Moderate
1	Very Infrequent (1 per year)	Nil Effect	High

Phase Three – Identifying Contributory Factors

A focus group was conducted where all stakeholders met to identify contributory factors for all failure modes in the entire pathway. The '5 Why' methodology was used to perform the analysis, whereby the question 'why' was repeatedly asked to identify the underlying contributory factor to a particular problem. This iterative technique was originally devised by Toyota for quality improvement and is endorsed by the WHO[14] and NHS Improvement for performing Quality and Service Improvement activities.[15] The discussion followed the chronological order of the CEA pathway, with emphasis on highest-scoring process steps.

Phase Four – Recommending Interventions

Once contributory factors were identified for each failure mode, the panel recommended interventions that may be implemented to prospectively prevent failures.

Results

Phase One – Observation

Ten patients were observed for 1,072 hours over 6 weeks, with 51 process steps identified in the carotid surgical pathway (including inpatients and outpatients).

As mentioned in Chapter 3, there were 110 patient safety incidents where harm or potential harm may have occurred – a rate of one incident approximately every 10 hours. In total, 10 (9.1%) were adverse events (any unintended injury that occurred), 66 (60.0%) were serious incidents (events with the potential to cause harm) and 34 (30.9%) were non-critical events (inconveniencing incidents from a patient's perspective). Half of patients experienced an adverse event between symptoms and discharge following CEA.

Phase Two – Risk Assessment

All 51 process steps were subdivided into three groups for ease of reference. The 'Diagnostic' pathway consisted of 12 steps, the 'Stroke Medicine' pathway consisted of 9 steps and the 'Vascular Surgery' pathway consisted of 30 steps.

The entire pathway, scoring matrix, failure modes, effect(s) and mean scores for frequency, severity and detectability (with mean hazard scores) are detailed in Appendix VII.

Mean hazard scores varied from 2.30-19.72. Table 4.2 shows the 5 highest-scoring failure modes, their effect(s) and mean scores for frequency, severity and detectability (with mean hazard scores).

Table 4.2: Highest scoring failure modes, their effect(s) and mean scores for frequency, severity and detectability (with mean hazard scores).

Rank	Process Step	Failure Mode(s)	Effect	Mean Frequency	Mean Severity	Mean Detectability	Mean Hazard Score (F x S x D)
1	Patient experiences symptoms	Patient does not recognise symptoms as stroke	Delay in seeking medical assistance	2.75	3.38	2.13	**19.72**
2	Patient/family member/friend calls Ambulance	Patient/family member/friend does not call Ambulance	Delay in clinical assessment	2.38	3.13	2.50	**18.55**
3	TIA Clinic Coordinator calls patient to schedule appointment	Patient does not answer their telephone/has a commitment on the suggested date	Delay in being assessed by Stroke Consultant	2.50	3.13	2.13	**16.60**
4	Patient transferred to HASU (inpatient)	Patient not transferred to HASU	Potential for mismanagement	1.88	3.38	2.25	**14.24**
5	TIA clinic referral made (outpatient)	Referral does not arrive/arrives over weekend or Public Holiday	Delay in being assessed by Stroke Consultant	2.38	2.75	2.13	**13.88**

Abbreviations – D: Detectability; F: Frequency; HASU: Hyper-Acute Stroke Unit; S: Severity; TIA: Transient Ischaemic Attack.

Phases Three and Four – Focus Group Discussion and Recommendations

65 organisational failures were identified from 51 process steps. These were prevalent throughout the pathway and sometimes recurred in different process steps. Following discussion, contributory factors for organisational failures were summarised into 5 themes:

1. Lack of patient understanding to recognise stroke symptoms (especially amaurosis fugax) and failure of GPs, ED Physicians and Opticians to recognise subtle neurology;

2. Inadequate, ineffective resource allocation (e.g. lack of hospital staff, especially out-of-hours; lack of ambulances, Porters, CT/MRI scanners, vascular/HDU beds; limited provision of weekend TIA clinic; inadequate length of GP appointments; unreliable hospital transport; and excessive parking charges) and lack of centralisation of services;

3. Limited use of technology to increase efficiency of documentation, streamline care and improve patient safety (e.g. electronic patient records with a user-friendly interface; electronic prescribing; and virtual appointments via Skype/FaceTime);

4. Lack of protocol-driven, standardised, Consultant-led care with occasional reluctance to embrace a culture of non-hierarchical, MDT working;

5. Inadequate communication between healthcare professionals (e.g. GPs and Consultants or between Specialists) when making referrals, between Specialists and patients when arranging reviews or dates for CEA and between the Trust and Junior Doctors during induction.

Organisational failures, contributory factors and recommendations for improvement are discussed in detail below as they relate to community care, ED assessment, Stroke team assessment, vascular assessment, peri-operative and post-operative care.

Community Care

Organisational Failures

The most important organisational failure identified in the community was patients not recognising their neurological symptoms as a stroke. GP Practices being closed on weekends and Public Holidays, GPs not returning patients' calls and both GPs and Opticians failing to recognise subtle stroke symptoms were also highlighted as failures in community care. Patients or their family member or friend failing to call an ambulance or driving to a hospital without a HASU were patient factors contributing to failures in the community.

Contributory Factors

Several factors were suggested as contributing to patients failing to recognise their stroke symptoms. This may partly be due to "complete ignorance" as symptoms "didn't match up to expected stroke symptoms". Patients "didn't think eye symptoms were stroke symptoms as the FAST campaign doesn't talk about eyes" and there was "no weakness or drooping". Symptoms also "went away quickly – if they had lasted more than 5 minutes, I would have been more worried". It was also suggested that the FAST campaign may not be pervasive enough as "the time from symptom onset to seeking medical advice seems to be getting longer". "Alternative diagnoses" may also make recognising a stroke difficult as "there are other things you can put it down to such as sleeping funny or migraines".

Problems with GP access may be due to the Practice being closed out-of-hours or on weekends and Public Holidays whilst GPs may not return a patient's call if their "workload is too much" and "sometimes things get missed". GPs and Opticians failing to recognise stroke symptoms may be because "patients do not always give a full history of their symptoms" or they may have "subtle or atypical symptoms or alternative diagnoses (e.g. Ménière's disease)". Also, "retinal photographs may not be accessible to people without paying", providing an additional barrier to relevant investigations.

Patients or their family member or friend may not call an ambulance, despite suspecting a stroke because they "don't want to waste anybody's time" or "bother ambulance services unless it is a life-or-death situation". They perceive a stroke as a "non-life-threatening illness" and there is a "campaign discouraging patients to attend ED with non-life-threatening illnesses". They also recognise ambulance services are short-staffed and "take hours to arrive" as stroke is a lower priority ("6 hour window for responding"). Another reason for not calling an ambulance may be that the patient's symptoms resolve so they can "see the GP instead" or their relative may drive them to ED. However, patients recognise that "ED is busy, we will have to wait hours, parking is extortionate and a nightmare as it costs a lot of money", potentially preventing them from seeking medical advice. They may also drive to a hospital that does not have a HASU due to "ignorance".

Recommendations

Education was suggested to improve stroke symptom recognition by patients. It was recommended that "it needs to be highlighted that if you have a blockage in your eyesight, it needs instant attention and to go see your GP or a hospital". Incorporating eye symptoms into the FAST campaign, with emphasis on "transient visual loss in one eye" as a specific symptom

of amaurosis fugax and also providing statistics regarding the recurrent stroke risk ("50% of strokes following TIA occur in the first 24 hours"), was suggested. Moreover, media campaigns such as uncoordinated Balance, Eye symptoms, FAST (BEFAST) may be helpful (including videos on television, advertisements in newspapers and posters in GP Practices and Opticians). However, these require re-emphasis at a public health level. It was also recommended that patients should be encouraged to call 111 for advice.

Improvements in accessing Primary Care services may be possible by having an "automated message to call 111" when calling the GP Practice out-of-hours. Virtual appointments via Skype or FaceTime were also recommended. Longer appointment times were expected to help GPs detect stroke symptoms more effectively as was "education of GPs and Opticians to pick up subtle or atypical symptoms". Use of local or College guidelines may also aid diagnosis as would eliminating paying for retinal photography.

Media campaigns to encourage patients to present to ED if they think they are having a stroke and to change the priority of a stroke diagnosis for ambulance responses were suggested. Moreover, "more staff and funding for ambulances and paramedics" and "educating and directing patients regarding accessing services" was suggested. "Abolishing parking charges", "improving public transport links" and "forming a dedicated ED car park with more spaces" was also recommended.

Regarding two-site working, "establishing links between different sites whilst maintaining a minimum standard for stroke services" was suggested as "the 'therapeutic step' can be delivered in few centres but the 'diagnostic step' can be made in all centres". However, it was thought more effective to centralise services as "we cannot provide top quality service across 2 sites close together" and "we need centres of excellence".

ED Assessment

Organisational Failures

The main failures associated with ED care were patients not being triaged, stroke diagnosis not being made and brain imaging not being performed.

Contributory Factors

Suggested reasons for lack of triage was "lack of senior decision-making" if the Triage Nurse was "not experienced enough" or "diagnostic uncertainty" surrounding atypical presentations. "Long waits in ED" may also contribute to difficulties with triage as "there are lots of patients waiting to be seen, often on trolleys". "Chaos" in ED was hypothesised to be due to "too big a population and not enough Doctors" as the job involves "unsociable hours, long shifts and poor work-life balance". "Atypical presentation" or "diagnostic uncertainty" was also suggested as a major cause of missing a stroke in ED, compounded by the "lack of staff and capacity issues" as there are "not enough bodies".

Cultural issues were identified as barriers to getting brain imaging in ED. Some panel members suggested that "some Radiologists need to be spoken to by a Consultant or Doctor before accepting a CT head request as they feel nervous receiving requests from Stroke Nurses" and "some Radiographers need to be spoken to separately". This introduces delays. There can also sometimes be "difficult Radiologists or Radiographers", making the process of requesting imaging more arduous. Other reasons identified included "lack of capacity" for CT and MRI scans as "there are not enough staff or machines and the CT scanner also breaks down sometimes". This is compounded by "more unwell patients needing urgent scans". Conversely, if the ED Doctors think that the patient's symptoms have resolved and they will be seen the

following day by the Stroke team, they will apply "personal clinical judgement" and may not do CT brain imaging in ED, especially out-of-hours. Moreover, there are "lots of portering issues" as there are "not enough Porters" so Clinicians "find a Healthcare Assistant or a Doctor to take the patient for their scan".

Recommendations

A "Consultant-led Rapid Access triage system with no juniors in the triage area" was suggested by the panel. This could be supplemented by a trained Triage Nurse who is supported by "pathways and protocols" and "Senior Nurses initiating imaging". It was felt that more staff and funding was required, especially to set up a "24/7 Consultant or Specialist-led service". "Education of ED Physicians to recognise vague TIA and stroke symptoms" and being able to "get a Carotid Doppler done in ED" would also be beneficial.

A "culture change" towards embracing a non-hierarchical MDT philosophy in managing patients was deemed essential for reducing barriers to effective patient care. Alteration of protocols to streamline care was also recommended. More funding was deemed necessary to employ more Porters, Radiologists and Radiographers whilst also increasing the number of CT and MRI scanners to provide a 24-hour service.

Stroke Team Assessment

Organisational Failures

Failures associated with Stroke team assessment included the patient not being referred to the Stroke team or transferred to the HASU, delays in patients being reviewed by the Stroke

Consultant, patients not answering their telephone to arrange their TIA clinic appointment or being unable to attend on the suggested date, no space for imaging requests (especially out-of-hours) and Stroke Consultants failing to alter patients' medications following review.

Contributory Factors

Handover was identified as a key problem. Referrals may not be sent to the Stroke team due to "lack of awareness about who to contact or how, especially for GPs and following changeover of Junior Doctors" due to the numerous methods for referral (face-to-face discussion, fax, e-referral or telephone). "Faxing errors", "forgetting to fax referrals at the end of a shift", the "electronic system breaking down" and "e-referrals being cumbersome to fill out" were also barriers to effective communication. GPs suggested that there was "not enough time in a 10-minute consultation to see the patient, download the form, fill it in, find the email address of the person to send it and then send it". This may lead to "poor communication of history in a referral letter" to the Stroke team where the patient had "more symptoms than mentioned in the letter", resulting in the patient being triaged as a lower priority to be seen in TIA clinic than they should have been, introducing delays.

Once reviewed in TIA clinic, a Stroke Consultant may fail to alter the patient's medications because of a "lack of computer literacy or problems with access to electronic prescribing". Patients themselves may be reluctant to change their medications and would "rather discuss it with their GP" or may be uncertain of their allergy status, "putting Consultants off prescribing".

The panel suggested that patients may not always be transferred across to the HASU due to "transport issues" and "Minor Injury Units may not be aware of services provided in hospitals". This is compounded by Switchboard putting callers through to the wrong person (e.g. Stroke

Ward Nurse instead of Stroke Specialist Nurse) and a lack of signal in the hospital for the telephone that the Stroke Specialist Nurse carries.

Patients may not attend their TIA clinic appointment as they ignore the call because they "didn't realise it was the hospital calling due to the 'unknown number' label" and being "suspicious of cold calling". They may also "misunderstand the severity of the condition" and do not expect to be contacted so quickly. The TIA Clinic Coordinator may have the wrong number or it "goes straight to voicemail" whilst occasionally it is "too short notice" for the patient to attend TIA clinic as they are "going on holiday", have "family commitments" or they have "nobody to bring them into hospital if it is a long distance to travel".

Possible reasons for limited access to imaging requests out-of-hours may include "lack of staff for Carotid Dopplers, especially at weekends". One panel member has been "asked not to request too many Carotid Dopplers" as they are "three staff members short in Gloucestershire". There is also limited access to CT angiograms due to insufficient Vascular Radiologists, Stroke Nurses cannot request this imaging modality and a greater radiation and contrast dose is required than conventional CT brain imaging.

Recommendations

A key recommendation was to streamline referrals by phasing out faxes, increase use of electronic patient records that are linked to Primary Care and create a self-populating, standardised, "tick box" e-referral form. Audit of this system with real-time feedback may minimise missed referrals. The electronic system should be user-friendly, robust, contain failsafe mechanisms and new Doctors would need to have an effective induction to maximise its functionality. This could be supplemented with a Single Access telephone number that

would be answered 24-hours by a Specialist Nurse who could confirm the time and date of the patient's appointment as written on their discharge summary in case of confusion. Together with electronic prescribing, this would allow patients' medications to be altered in the clinic room and better documentation of their allergy status.

Minor Injury Units should be educated in the services provided by hospitals so patients are sent to the correct location based on their presenting complaint. Switchboard should also be educated on the best contact if an external caller asks to speak with a member of the Stroke team for advice or HASU transfer. Upgrading telephone signal in the hospital or providing a specific bleep number or pre-alert landline telephone was also recommended.

Improving hospital transport and increasing GP appointment times to improve quality of referrals were recurrent recommendations. Having a Stroke Consultant available 24-hours for TIA and stroke referrals was also suggested (especially in District General Hospitals).

It was also recommended to reveal the telephone number or show the label 'Hospital Switchboard' when calling patients to schedule TIA clinic appointments. Better communication with patients, advising that they will be contacted within 24 hours of the referral being sent and double-checking their telephone number with them (or their GP Practice or Care Home) may reduce the incidence of having the wrong number. A confirmatory text message after the appointment has been scheduled was also recommended as was GPs calling the TIA Clinic Coordinator "with the patient in the room to arrange an appointment" or "Stroke Consultants policing their own diaries to make space in clinic for urgent referrals".

Issues with access to imaging may require extra funding to employ more Vascular Scientists, Radiologists, Radiographers and Porters. Allowing Stroke Specialist Nurses to request CT angiograms may lead to more scans being performed. Incorporating training in performing Carotid Dopplers into the Vascular Surgery training programme may also be helpful.

Vascular Assessment

Organisational Failures

Organisational failures, identified in other areas of the pathway, were referrals not arriving or arriving out-of-hours, Stroke Consultants not discussing referrals with Vascular Consultants so the latter fail to recognise their urgency, patients not answering their telephone for their vascular review appointment or not being able to attend on the suggested date. Other failures included Vascular Consultants not reviewing patients on the HASU, difficulties transferring patients to the vascular ward, medical notes sometimes being unavailable and Vascular Consultants not always discussing patients in the MDT meeting prior to surgery.

Contributory Factors

It was suggested that there would be delays if referrals arrived over the weekend or on Public Holidays as administrative staff do not work out-of-hours. Moreover, "complexities can be missed in a short, snappy e-referral", which may contribute to Vascular Consultants failing to recognise the urgency. A cultural issue was also identified whereby some Vascular Consultants were occasionally reluctant to receive referrals from administrative staff and "preferred receiving referrals from Stroke Consultants directly so they could ask relevant questions".

Reasons for delay in vascular review included a "theoretical risk of being swamped with urgent operating so the review gets delayed" and, as previously discussed, patients may have other commitments (e.g. holidays or family commitments) or "not grasping the urgency of needing to be seen by the Vascular Consultant". "Elderly patients find long distances physically hard to travel" and "hospital transport is not good and unreliable, often not turning up". There was a reluctance from Vascular Consultants to review patients on the HASU as the journey between

Cheltenham General Hospital and Gloucestershire Royal Hospital takes “40 minutes one way” and the Consultant is “slightly vulnerable if something were to go wrong in the hub”. However, it was also thought that it is “laborious to arrange patient transfers as vascular beds can’t be ringfenced” (the process being described as “a bit of a rigmarole”) and is “more of an ordeal for the patient to be moved across sites”.

Medical notes were not always available for vascular review and would be “useful in complex patients” as referrals sometimes contain “limited information”. An MDT discussion was also not standard practice as there were indirect contacts between the Vascular Consultant and Stroke Physicians, Vascular ANPs, Anaesthetists and Radiologists through “standardised protocols”. However, there was potential for error from communication issues.

Recommendations

It was suggested to implement a shared inbox for e-referrals as a “single point of access” for Coordinators, Secretaries and Supervisors to act on referrals and audit practice. Providing feedback to the referrer when the referral was received and advising dates of vascular review and CEA may also be helpful. Whilst e-referrals worked well, it was recommended education is provided to referrers regarding the amount and type of information that is useful and that Stroke Consultants discuss “ambiguous patients” with Vascular Consultants. However, the panel recognised the need for a “cultural shift” to embrace MDT patient management.

A “Carotid Consultant” may mitigate against the ‘Consultant of the Week’ being too busy with emergency operating to perform reviews whilst educating patients in understanding the severity and consequences of their symptoms (involving GPs in correspondence) may further reduce delays. Improving hospital transport or public transport links may also be helpful.

Co-location of stroke and vascular services was a key recommendation to eliminate issues with transferring patients between Gloucestershire Royal Hospital and Cheltenham General Hospital. The ability to "ringfence vascular beds" and "streamline transfers" was also thought to be helpful. This may also help ensure medical notes were available for all reviews.

The panel also recommended providing information leaflets to patients explaining that CEA is "prophylactic surgery" and that they may "derive no real tangible benefit from the intervention and actually feel worse rather than better in the short-term". Standardising the process of sending a letter to the referring Stroke Consultant, GP and patient following vascular review may also improve communication.

Peri-operative Care

Organisational Failures

Peri-operative care was thought to be high-quality. Organisational failures identified included delays in pre-operative assessment, CEA being cancelled, delayed or the date being miscommunicated, difficulties in transferring patients to Operating Theatre and patients not being admitted to Recovery or HDU post-operatively.

Contributory Factors

Delays in pre-operative assessment may be due to "waiting for specific investigations (e.g. stress echocardiogram or angiogram)" or "engaging with other specialties for opinions" whilst "miscommunication" can cause "patients to get dates mixed up".

Portering issues may delay patient transfer to Operating Theatre whilst staffing and funding issues may lead to "no HDU bed or capacity in Recovery" to accommodate patients requiring close monitoring following CEA. Ineffective communication between Anaesthetists, Surgeons and Intensivists during pre-operative planning may exacerbate this situation.

Recommendations

Standardising pre-operative assessment and close working between Specialists with established protocols may reduce delays in scheduling CEA. "Safety netting" by asking patients to call the vascular ward or Secretary the day before their CEA to confirm arrangements and check bed availability may empower them and allow rescheduling.

However, the key recommendation was more staff and funding (for more beds and capacity) in HDU and Recovery and more Porters. Better communication between Anaesthetists, Surgeons and Intensivists during pre-operative planning was also deemed essential.

Post-operative Care

Organisational Failures

Post-operative care was thought to be high-quality. Organisational failures included ward round entries and operation notes not being documented clearly, confusion regarding post-operative medications, lack of Vascular Consultants and delays in discharging patients.

Contributory Factors

Ward round entries and post-operative instructions were hand-written and sometimes one "can't read what the Clinician has written", causing confusion. Moreover, regarding post-operative anti-platelets, "the protocol is not standardised between Consultants". There are also multiple systems in use which means that "things can get missed" and it can be "a bit of a struggle", especially when the "printer is malfunctioning".

It was suggested that there may be risk to patients if 2 emergencies presented at the same time for the on-call Vascular Consultant, each of equally high priority. In this scenario, the ward patients would also be delayed in being reviewed or would be seen by a less experienced team member.

The process of discharging a patient was not thought to work well. Discharge summaries were a "low priority" for Clinicians and too "target-based", often containing "pages of useless information". There were also "huge delays" in repatriating patients to the Stroke Rehabilitation ward following successful CEA as the receiving ward gets a "lower tariff compared to admitting an ED patient". "Limited service over the weekend" of Occupational Therapists and Physiotherapists also contributed to "problems with speed of discharge".

Recommendations

As previously suggested, the panel recommended implementation of streamlined electronic patient records with regularly maintained equipment to improve clarity of documentation and communication. Standardising post-operative care in a protocol was also thought to be helpful. Integral to these changes would be a culture change to embrace standardisation of care (including handovers) and the use of electronic patient records. A formalised system for a 2nd

on-call Consultant (requiring more staffing and funding) may also mitigate against patient harm in the case of a major incident.

Streamlining discharge summaries using electronic patient records and changing the culture of writing discharge summaries from a "tick box exercise" to emphasising its clinical utility was deemed necessary. This may require a change in hospital remuneration. Completing discharge summaries earlier in the day (beginning them in Operating Theatre) and formalising an agreement to repatriate patients to the spoke within 72 hours of being surgically fit for discharge may improve efficiency of discharges. This may also require a change in hospital remuneration. Recruiting more Occupational Therapists to work over the weekend and "incentivising each discharge completed out-of-hours with performance-based bonuses" may further improve the efficiency of the discharge process.

Providing patients with a telephone number to contact the Surgical team if they have any concerns post-operatively and scheduling outpatient appointments prior to discharge (and providing patients with details) may ensure more effective follow-up.

Discussion

This HFMEA that assessed the carotid surgical pathway of symptomatic patients, from experiencing symptoms to being discharged following CEA (in outpatient and inpatient settings), identified 65 organisational failures in 51 process steps. This led to recommendations in 5 areas: improve patient understanding to recognise stroke symptoms whilst also educating GPs, ED Physicians and Opticians to recognise subtle neurological symptoms; improve resource allocation to allow centralisation of stroke and vascular services; implement latest technology to improve documentation, streamline care, enhance efficiency and patient safety; use protocol-driven, Consultant-led care to standardise practice in a culture of non-hierarchical, MDT working; and improve communication between healthcare professionals (including effective handovers and inductions) and also with patients. These recommendations should be implemented in hospitals with their effect on improving outcomes in these high-risk patients monitored by clinical audit. If shown to be effective, findings from this study may allow an optimised CEA pathway to be constructed for symptomatic patients in the future.

Patient Education

Patients not recognising their stroke symptoms was the highest-scoring failure mode according to our panel. This was supported by no patients realising they were having a stroke/TIA when they experienced their neurological symptoms, with three patients delaying presentation to medical services until they had recurrent neurological episodes. This was deemed to be a failure of public health and patient education was recommended, particularly by incorporating eye symptoms into the FAST campaign. However, effectiveness of pre-hospital stroke detection was not improved with BEFAST compared with FAST.[16] Whilst BEFAST had a higher

sensitivity than FAST (91% versus 76%), it had a lower specificity (56% versus 68%) and similar positive predictive value (49% versus 53%).[16] This may be because balance and eye symptoms were not independent predictors of stroke in the authors' multivariate analysis, causing 4 extra stroke-mimics per 100 patients to be falsely identified by BEFAST compared to FAST criteria.[16]

Public knowledge regarding stroke is inadequate, with 38% recognising stroke symptoms and 25% identifying their own symptoms.[17] In one study, 27% of patients interviewed could not name a single stroke symptom.[18] In the UK, a systematic review reported that patients recognised unilateral weakness and speech disturbance as stroke symptoms but less than half identified themselves having a stroke.[19] Media campaigns such as FAST increase knowledge about stroke symptoms and the need to present early to ED.[20] However, this increased awareness was not sustained after the campaign ceased in Canada.[20] A German multimedia campaign (in newspapers, television, radio, leaflets and advertisements) also failed to change care-seeking behaviour (despite improving knowledge) with similar proportions of patients calling an ambulance after suffering stroke symptoms before and after the campaign.[21]

Various studies have investigated using different educational modalities to improve stroke recognition. Stern *et al*.[22] combined audio and slides (12 minutes long) to target individuals aged above 50 years and at risk of stroke, living in the community. They reported improvement in knowledge of stroke risk factors, symptoms and action in 657 adults.[22] Similarly, Rodgers *et al*.[23] randomised 204 acute stroke patients to receive a 1-hour inpatient seminar followed by 6 one-hour sessions in the community or no education. Test scores at 6 months were significantly higher for the group that received the intervention (n=121) compared to controls (n=83).[23] However, this study was underpowered and it may not be feasible to implement intensive educational programmes. De Lemos *et al*.[24] performed a community educational

programme including health screening and stroke education, resulting in a 35% increase in knowledge of stroke symptoms but this declined by 17% at 3 months post-intervention.[24] No lifestyle changes were made by 64% of participants following the intervention and no smokers stopped smoking.[24] Chan *et al*.[25] performed focussed stroke education in an ED waiting room to capture a large audience. Education via video, counselling, brochure and a combination of all modalities significantly improved stroke knowledge.[25] However, this was not sustained at 1 month, with the combination educational modality being most effective and the video group least effective.[25] Therefore, it is important to improve education of stroke symptoms at a public health level and use multiple modalities (video, newspapers, television, posters and/or leaflets) to encourage patients to seek urgent medical attention if they experience stroke symptoms. Sustaining initial improvements in stroke knowledge following implementation of educational programmes will be the challenge that needs to be effectively overcome.

Resource Allocation

Inadequate resource allocation was identified as a root cause for lack of staff (especially out-of-hours), ambulances, Paramedics, Porters, CT/MRI scanners and HDU beds whilst it may have contributed to limited provision of weekend TIA clinic, GPs feeling their appointments were too short and unreliable hospital transport for patients. These insights support an analysis by the King's Fund comparing the NHS with health services in 20 other English-speaking countries across the Organisation for Economic Cooperation and Development (OECD). They reported that the UK has fewer Doctors (2.8 per 1,000 population; average: 3.6) and Nurses (7.9 per 1,000 population) than other countries included in the analysis, except Poland.[26] This is below OECD and European Union (EU) averages and considerably lower than countries of similar economic development.[27] By comparison, Germany has 13.3 Nurses per 1,000

population and Switzerland has 18 Nurses per 1,000 population.[26] The UK also has fewer CT and MRI scanners per capita than any OECD country analysed whilst also having fewer hospital beds per capita than any other country, except Denmark and Sweden.[26] The UK has 2.6 beds per 1,000 population (below the OECD average of 4.7 and the EU average of 4.8 beds per 1,000 population) as a consequence of the number of hospital beds in England reducing by more than half over the last 30 years.[26, 27] The resulting increased hospital bed occupancy (more than 90% in a recent analysis and above the recommended 85% threshold for safe and efficient care) reduces patient flow and increases waiting times for urgent and planned treatment.[26] The UK also spends 9.7% of its Gross Domestic Product (GDP) on healthcare (average for countries analysed but less than Germany and France, who spend more than 11.0% of their GDP on healthcare).[26] UK investment in healthcare as a proportion of GDP was also lower than the pooled average of Australia, Canada, Denmark, France, Germany, Holland, Sweden, Switzerland and the USA (all fellow members of G12), which may have contributed to a decline in health service outcomes and the overall health of the population, as reported in a recent observational study.[27]

To address this funding gap, the UK Government has pledged to increase NHS funding by £20.5 billion in real terms per year from 2018-2024.[28] This is an average increase of 3.4% in funding that is front-loaded in the first 2 years.[28] The UK Government outlined how this additional funding would be used in its *NHS Long Term Plan*, published in January 2019.[28]

One of the key pledges by the UK Government was to alleviate ED pressures by forming 'urgent treatment centres' and encouraging 'same day emergency care' for those that need hospital management of illnesses, aiming to increase the proportion of acute patients discharged on the same day of admission from 20% to 33%.[28] This was also encouraged in the GIRFT report for Vascular Surgery[29] and may help reduce ED pressures identified in our study.

Investment in ambulance services has also been promised to ensure timely and effective responses. A ringfenced sum of £4.5 billion has been allocated to create local GP networks with expanded community MDTs, encouraging more effective management in the community.[28] This may reduce pressures on GPs, potentially preventing stroke diagnoses being missed and increasing time for making more effective referrals.

Specifically for stroke care, the UK Government has suggested centralising services, as our panel recommended. These 'Integrated Stroke Delivery Networks' will ensure seven-day standards for stroke care, including improved ambulance services and early supported discharge through improved stroke rehabilitation.[28] The *NHS Long Term Plan* also encouraged improved access to thrombolysis and thrombectomy.[28]

The GIRFT and VSGBI reports also suggested centralisation of vascular services into hubs and spokes, as previously discussed, to pool available resources and staff whilst allowing an MDT approach to managing patients in a standardised and protocol-driven fashion.[29, 30] This would also enable reconfiguration of vascular operations as urgent, enabling 7-day operating, reducing delays for CEA.[29] The GIRFT report suggested reducing time from symptoms to surgery from 14 days to 7 days.[29] This would require increases in the workforce of Consultant Vascular Surgeons to account for challenges in population growth (especially elderly and more co-morbid patents) and changing work patterns (e.g. less than full-time working and 7-day working). Currently, the ratio of UK Consultant Vascular Surgeons is 1 per 137,000 population, which is lower than comparative countries in Europe, Australasia and North America.[29, 30] The VSGBI recommended increasing this to 1 per 100,000 population, requiring a minimum of 6 Vascular Consultants in a Department to run surgical lists 7 days a week.[29, 30] Our panel also suggested increasing the number of Vascular Consultants, even though Cheltenham General Hospital Vascular Department had 7 Consultants.

The *NHS Long Term Plan* also pledged a workforce implementation plan to expand the numbers of Nurses (by 5,000) and Doctors (including 5,000 GPs) working in the NHS to combat the 100,000 clinical staff vacancies across the NHS.[26, 28] This is a key recommendation from our HFMEA analysis to relieve workplace pressures and their effect on patient care, especially given that there has been an 87% reduction in Nurses coming from the EU to work in the UK between 2016-2017 and 2017-2018.[31] This is likely to be further exacerbated following the UK's departure from the EU. The number of volunteers working in the NHS will also be doubled over the next 3 years with a further £2.3 million investment.[28] These volunteers can be vital in ensuring a smooth patient journey through the hospital and may improve patient experience of the care they receive.

Harnessing Technology

Our panel recommended harnessing the power of technology to improve documentation, communication and streamline care, improving efficiency and patient safety. The *NHS Long Term Plan* suggested that patients will have access to online 'digital' consultations within 5 years, in keeping with our panel's recommendations.[28] This is estimated to reduce the number of outpatient appointments by one-third and pressures on GPs, saving 30 million trips to hospital and the NHS £1 billion per year.[28] A new 'NHS App' will also provide advice, allow checking of symptoms and connections with healthcare professionals via telephone and video consultations.[28] This may help patients detect stroke symptoms more effectively.

Technology will also be implemented in the specific management of stroke patients. By using latest imaging modalities such as CT perfusion scans and MRI scanning with Artificial Intelligence (AI) interpretation, stroke diagnoses may be expedited.[28] Telehealth may also

allow more efficient communication and information sharing between providers (e.g. Paramedics and ED Doctors), improving effectiveness of hyper-acute pathways for patients to access timely care.[28, 30] These policies are in keeping with our panel's recommendations to improve outcomes in stroke patients.

Effective implementation of technology was also recommended by our panel to aid Clinicians in their daily work. The *NHS Long Term Plan* has pledged to ensure Clinicians can access patient records more easily by reducing the burden of managing data flows between different Trusts and systems.[28] Greater inter-operability and streamlining digital platforms would allow Clinicians to spend more time and resources treating patients.[28] Incorporation of AI and decision-support tools may also aid application of evidence-based practice and eliminate unnecessary variation in care that may harm patients.[28]

Digitalisation of patient notes with electronic prescribing was also an important recommendation by the panel to improve documentation and communication. The *NHS Long Term Plan* has promised to eliminate use of fax machines in the NHS by 2020 and implement "robust, modern Information Technology infrastructure" regarding electronic patient records.[28] All NHS Trusts will be expected to meet this requirement by 2024.[28] This should improve quality of referrals and may allow access to Specialist advice virtually, without an outpatient appointment. Electronic patient records may also allow electronic prescribing, with prompts to avoid dangerous interactions or highlighting relevant patient allergies. This may explain why electronic patient records significantly reduced documentation time ($p<0.007$) and medication errors ($p<0.001$) in a systematic review.[32]

Standardising Care

Minimising variation in patient management by standardising care through protocol-based, Consultant-led care (in an MDT working culture) was identified by our panel as a priority to maximise the quality of care delivered to stroke patients. The Care Quality Commission (CQC) published a report called *Opening the Door to Change: NHS Safety Culture and the Need for Transformation* that suggested greater standardisation of processes may reduce pressure on Clinicians.[33] However, it was recognised that not all processes can be standardised and would require collaboration between NHS Improvement, Professional Regulators, Royal Colleges, Clinicians and patient groups to identify processes that would benefit from standardisation and ensure they are evidence-based and effective.[33] Due to a lack of confidence in standardisation of clinical processes, staff would be encouraged to speak up when processes were flouted but professional judgement should be used where necessary by appropriately qualified and experienced team members.[33]

One area our panel thought may benefit from standardisation would be to harmonise internal processes that may contribute to delays in patients undergoing CEA. For example, by using protocols to streamline referrals, imaging and reviews prior to discharge, this may improve the efficiency of the CEA pathway. This recommendation was also suggested in the GIRFT report, with emphasis on using cross-departmental referral pathways to expedite reviews by other medical specialties and discharge planning protocols with achievable timescales to reduce delays in obtaining Physiotherapy and Occupational Therapy input.[29] Access to seven-day Physiotherapy services, as part of an MDT package of individualised support with recovery post-surgery, was also suggested in the GIRFT report.[29]

The CQC also identified that hierarchies have detrimental effects on an organisation's safety culture and should be flattened.[33] This has been recognised by other industries. For example,

British Airways performs simulation training in an MDT environment to reduce hierarchies and encourage staff to appreciate roles of other team members.[33] Specifically for stroke patients, establishment of acute frailty services to support patients undergoing CEA would be in keeping with the MDT working culture recommended by our panel.[28]

Strengths

This study is the first HFMEA analysis of the carotid surgical pathway of symptomatic patients to date, from experiencing symptoms to being discharged following CEA. It identified 65 organisational failures in 51 process steps in the pathway following 1,072 hours of ethnographic observation. This has highlighted important issues that have not been identified previously, including patients failing to recognise their stroke symptoms as a public health failure, patients presenting with stroke symptoms to a hospital without a HASU, problems with communicating referrals between Specialists, issues with contacting patients to arrange outpatient reviews and inefficiencies in the discharge process.

Various studies have used HFMEA to prevent harm in surgical patients.[9-12] Johnston *et al*.[9] used HFMEA to improve escalation of care in General Surgery patients. Similarly, Anderson *et al*.[10] undertook HFMEA to prospectively mitigate against adverse events occurring on surgical wards. Other studies have improved the quality of care of Bariatric patients[11] and the quality of training in Colorectal Surgery using HFMEA.[12] However, these studies have focussed on one aspect of the pathway. Our study analysed the entire pathway and suggested improvements in symptom detection and care in Primary Care, ED, stroke ward, vascular ward and outpatients. As many specialties care for symptomatic patients undergoing CEA, recommendations should target multiple aspects of the pathway for improvement.

The inclusion of 13 stakeholders to participate in the systematic risk assessment of the CEA pathway and focus group discussion is a particular strength of this study. Participants included at least one Consultant Stroke Physician, Consultant Vascular Surgeon, Consultant ED Physician, Consultant Anaesthetist, GP, Vascular ANP, Stroke Specialist Nurse, Vascular Coordinator, TIA Clinic Coordinator and a patient. They drew on their collective experience to provide meaningful insights to improve the pathway. An MDT panel allowed plurality of opinions, which were applicable throughout the pathway and the inclusion of a patient kept discussions and recommendations relevant. These recommendations may prospectively prevent adverse events occurring, a strength of HFMEA.

Limitations

Recommendations may not be applicable nationally. However, observations were conducted in 3 large, well-resourced hospitals whilst panel members were drawn from NHS Trusts across England (including Hampshire, Yorkshire and Gloucestershire), representing current NHS practice. Therefore, our recommendations are relevant but may need local application.

Another limitation may be that our recommendations include allocating further resources to the NHS, implementing latest technology, providing Consultant-led care and expanding stroke awareness campaigns to educate patients in detecting stroke symptoms. This degree of investment in the NHS may not be realistic in the current economic climate, particularly following the UK's departure from the EU. However, these suggestions are in agreement with analyses from the King's Fund[26], UK Government policy[28] and recommendations by the GIRFT and VSGBI reports.[29, 30] Short-term investment may lead to long-term savings if patient outcomes improve and healthcare is delivered more efficiently.

Conclusions and Implications

This HFMEA has, for the first time, assessed the carotid surgical pathway of symptomatic patients, from experiencing symptoms to being discharged following CEA (in outpatient and inpatient settings), and identified 65 organisational failures in 51 process steps. Recommendations from 13 stakeholders include: improving patient understanding to recognise stroke symptoms whilst also educating GPs, ED Physicians and Opticians to recognise subtle neurological symptoms; improving resource allocation to allow centralisation of stroke and vascular services; implementing latest technology to improve documentation, streamline care, enhance efficiency and patient safety; using protocol-driven, Consultant-led care to standardise practice in a culture of non-hierarchical, MDT working; and improving communication between healthcare professionals (including effective handovers) and with patients.

This study has shown the value and clinical utility of applying HFMEA to improve the quality of healthcare processes. Our findings suggest that structural factors can be optimised to improve the quality, safety and efficiency of care delivered to symptomatic patients undergoing CEA. Recommendations suggested in this analysis should be implemented in hospitals with their effect on improving outcomes in this high-risk group of patients monitored by clinical audit. If shown to be effective, findings from this study may allow an optimised CEA pathway to be constructed for symptomatic patients in the future.

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CHAPTER 5: Contemporary Procedural Risks in 19,000 patients undergoing Carotid Interventions in a Global Administrative Dataset

Abstract

Background: Procedural risks in historical randomised clinical trials (RCTs) may not generalise to current practice but large administrative datasets may provide more reliable estimates of contemporary risk. This study aimed to quantify rates of major complications following carotid intervention in an international benchmarking collaborative dataset, comprising 18,997 patients admitted to 28 hospitals across 7 countries.

Methods: Symptomatic and asymptomatic patients undergoing CEA (n=16,220) and CAS (n=2,777) between 2011-2015 were studied. The primary outcome was in-hospital death within seven days. Secondary outcomes were the computerised tomographic brain imaging rate (proxy for suspected or actual procedural stroke) and LOS exceeding two days (proxy for suspected or actual procedural complications).

Results: In symptomatic patients following CEA, in-hospital mortality was 0.2% (5/2,118; 95% Confidence Interval: 0.1-0.5), suspected stroke rate was 8.1% (89/1,101; 6.5-9.7) and the proportion with prolonged LOS was 57.0% (628/1,101; 54.1-60.0). In asymptomatic patients following CEA, mortality was 0.1% (21/14,102; 0.1-0.2), suspected stroke rate was 2.1% (207/10,039; 1.8-2.3) and the proportion with prolonged LOS was 28.5% (2,864/10,039; 27.7-29.4). In symptomatic patients following CAS, mortality was 3.3% (10/307; 1.3-5.2), suspected stroke rate was 7.1% (16/224; 4.0-10.7) and the proportion with prolonged LOS was 64.3% (144/224; 58.0-70.5). In asymptomatic patients following CAS, mortality was 0.7% (18/2,470; 0.4-1.1), suspected stroke rate was 3.2% (71/2,187; 2.5-4.0) and the proportion with prolonged LOS was 27.5% (601/2,187; 25.6-29.4).

Conclusions: Death, post-procedural brain imaging (proxy for suspected stroke) and prolonged LOS following carotid intervention were observed more frequently in symptomatic than asymptomatic patients. Symptomatic patients undergoing CAS had increased risk of death compared to those receiving CEA. This may be partly explained by case selection, where more co-morbid patients preferentially underwent CAS. Whilst RCTs are necessary to robustly compare long-term efficacy of CEA and CAS, large administrative datasets may provide more reliable estimates of contemporary procedural risks.

Introduction

This chapter will quantitatively analyse a large administrative dataset to assess CEA and CAS procedural complications. This will allow comparison with RCT findings and provide the basis for undertaking analyses in the larger HES administrative dataset in Chapters 6 and 7.

Background

RCTs are the 'gold standard' in comparing effectiveness of new interventions (medical or surgical) to established practice. When rigorously conducted, they have several advantages. Randomisation of individuals to the 'intervention' or 'control' group minimises bias and ensures that the 2 groups will be comparable in demographics, comorbidities and confounding factors whilst double-blinding minimises performance bias. Intention-to-treat analysis also minimises the effect of treatment switching or withdrawal on outcomes whilst meta-analysis of RCTs is the highest form of evidence and informs clinical practice.

However, CEA and CAS procedural outcomes reported in RCTs may not generalise to contemporary practice, especially as CMT, surgical devices and familiarity with their use has improved substantially since the first CAS trial started recruiting patients over 20 years ago. RCTs comparing CEA versus CAS also had varying use of EPDs and included Surgeons/Interventionalists with wide-ranging experience. Moreover, one RCT[1] excluded strokes lasting less than 7 days, confounding results, whilst another[2] only included patients at high operative risk. Therefore, RCT findings may not generalise to procedures performed in the wider community. RCTs also enrol less participants and capture fewer events than large registries. As CEA and CAS procedural risks are low, analyses of administrative data may have greater power to accurately describe contemporary estimates of procedural risks than RCTs.

Strengths of Administrative Datasets

Administrative data are usually collected for non-research purposes (e.g. HES data is collected for remuneration of hospitals). However, administrative datasets can be used for research to analyse large volumes of routinely collected, contemporaneous data. This provides reliability to the data. Large administrative datasets may also more accurately reflect the contemporary effect of advances in modern surgical practice and CMT on procedural outcomes following carotid intervention than results derived from historical RCTs. They usually contain more patients than RCTs and capture more events. The population included in registries will likely also include patients that were ineligible for inclusion in RCTs and may be more representative of the general population. However, using administrative data for research also has limitations.

Limitations of Administrative Datasets

Non-randomised data are added by Clinicians or hospitals (depending on the type of administrative dataset), which may introduce bias and coding errors. The researcher also cannot control what data are collected so items of interest may be unavailable. This may lead to confounding in subsequent analyses if all relevant covariates cannot be adjusted. The format of the dataset is usually not conducive for immediately performing analyses so reorganisation or 'data cleaning' is usually required. This can be time-consuming and laborious.

Therefore, analyses from administrative datasets should be carefully interpreted when applied to clinical practice. RCTs are the highest form of evidence when comparing long-term efficacy of interventions but analyses from administrative datasets may estimate procedural risks more reliably, with larger statistical power, and generalise better to contemporary practice.

Rationale for Study

We had access to a large administrative dataset, established as part of the Dr Foster Global Comparators' (GC) Project. This is an international, benchmarking, collaborating initiative that collects and shares data from institutions globally for quality improvement and identification of best practice, improving patient outcomes. This has been demonstrated in elective Colorectal Surgery[3] and emergency General Surgery.[4] It is a Clinician-led, not-for-profit subsidiary of Telstra Corporation©. There are 41 collaborating centres, across 4 continents, but the database is managed by analysts based in London. They liaise closely with contributing centres and receive quarterly data updates.

GC contains data relating to 18,997 patients who underwent CEA or CAS in 28 hospitals across 7 countries. Assessing procedural risks may help identify problems in using administrative data before analysing the larger HES dataset in Chapters 6 and 7.

Aim

This study aimed to quantify procedural complications (7-day in-hospital mortality; suspected stroke rate; and prolonged LOS) in symptomatic and asymptomatic patients undergoing CEA and CAS in an international, benchmarking, collaborative dataset.

Methods

Participants

Data were obtained retrospectively from GC centres in Australia, Belgium, Denmark, Finland, England, Holland and the USA, as previously described.[5] For English hospitals, further data were obtained from the HES dataset. For other countries, electronic patient records were used.

Data relating to median age, demographics, primary diagnosis and comorbidities (DM, obesity and IHD) were also collected.

All centres provided consent for use of their data for research. No identifiable patient data were used so consent from individuals was not required.

All patients who underwent CEA or CAS between 2011-2015 were included in this study. Centres were excluded if their dataset was incomplete. Any admissions not related to carotid intervention were excluded.

Study Outcomes

The primary outcome was 7-day in-hospital death post-carotid intervention.

Difficulties arose in accurately determining procedural strokes due to the coding method being unable to differentiate between patients who had suffered strokes prior to or following CEA or CAS. Therefore, CT brain imaging within 2 days of carotid intervention was used as a proxy measure for suspected or actual procedural stroke.[5]

The proportion of patients with a post-procedural LOS greater than 2 days was also analysed as a proxy for suspected or actual procedural complications.[5]

Statistics

Using International Classification of Diseases (ICD)-9 and ICD-10 codes for CEA and CAS, data from participating countries were collated and 95% CIs calculated for all outcomes. Cohort characteristics were compared statistically using the Chi-squared test, except for median age where the Mann-Whitney U test was used.

A p-value ≤ 0.05 was deemed statistically significant. All analyses were performed using the software package R, version 3.6.2 (The R Foundation for Statistical Computing, Boston, USA).

Results

A total of 16,220 CEA and 2,777 CAS procedures were included in this study. European centres (n=15) recruited 8,892 (46.8%) patients, American centres (n=9) recruited 8,363 (44.0%) patients and Australian centres (n=4) recruited 1,742 (9.2%) patients.

The median age of CEA patients was 71 (inter-quartile range: 64-77) years and 69 (inter-quartile range: 61-76) years for CAS (Table 5.1). The proportion of females was similar between CEA and CAS groups (34.4% and 36.0% respectively).

Indications and Comorbidities (Table 5.1)

The majority of patients undergoing CEA and CAS were asymptomatic (84.1% and 87.8% respectively). For symptomatic patients, ischaemic stroke was the commonest indication for CEA (13.1%) and CAS (11.1%). The percentage of patients with a TIA undergoing CEA and CAS was 2.8% and 1.1% respectively.

A slightly lower proportion of patients undergoing CEA than CAS had DM (23.5% and 28.2% respectively) and obesity (5.6% and 7.0% respectively). IHD was significantly more common in the CAS than CEA group (44.7% versus 28.4% respectively; p=0.01).

Table 5.1: Demographic details, primary indication (for symptomatic patients) and comorbidities listed for all patients undergoing CEA and CAS in the Global Comparators' dataset.

Procedural data	**CEA**	**CAS**	
Procedures (n)	16,220	2,777	
Hospitals (n)	28	23	
Demographics			
Median age (IQR)	71.0 (64-77)	69.0 (61-76)	p=0.40
Percentage Female	34.4	36.0	p=0.77
Primary Diagnosis (%)			
Symptomatic	15.9	12.2	p=0.41
Ischaemic Stroke	13.1	11.1	p=0.66
TIA	2.8	1.1	p=0.31
Comorbidity (%)			
DM	23.5	28.2	p=0.52
Obesity	5.6	7.0	p=0.77
IHD	28.4	44.7	***p=0.01***

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; DM: Diabetes Mellitus; IHD: Ischaemic Heart Disease; IQR: Inter-Quartile Range; TIA: Transient Ischaemic Attack.

CEA Outcomes (Table 5.2)

For symptomatic patients undergoing CEA, the 7-day in-hospital mortality rate was 0.2% (5/2,118; 95% CI: 0.1-0.5), the post-procedural CT brain imaging rate was 8.1% (89/1,101; 6.5-9.7) and the proportion of post-procedural LOS more than 2 days was 57.0% (628/1,101; 54.1-60.0).

For asymptomatic patients undergoing CEA, the 7-day in-hospital mortality rate was 0.1% (21/14,102; 0.1-0.2), the post-procedural CT brain imaging rate was 2.1% (207/10,039; 1.8-2.3) and the proportion of post-procedural LOS more than 2 days was 28.5% (2,864/10,039; 27.7-29.4).

CAS Outcomes (Table 5.2)

For symptomatic patients undergoing CAS, the 7-day in-hospital mortality rate was 3.3% (10/307; 1.3-5.2), the post-procedural CT brain imaging rate was 7.1% (16/224; 4.0-10.7) and the proportion of post-procedural LOS more than 2 days was 64.3% (144/224; 58.0-70.5).

For asymptomatic patients undergoing CAS, the 7-day in-hospital mortality rate was 0.7% (18/2,470; 0.4-1.1), the post-procedural CT brain imaging rate was 3.2% (71/2,187; 2.5-4.0) and the proportion of post-procedural LOS more than 2 days was 27.5% (601/2,187; 25.6-29.4).

Table 5.2: Study outcomes (with 95% CIs) following CEA and CAS, listed for both symptomatic and asymptomatic patients.

Rates (95% CI)	Symptomatic		Asymptomatic	
	CEA	**CAS**	**CEA**	**CAS**
7-day in-hospital mortality	0.2% [5/2,118] (0.1-0.5)	3.3% [10/307] (1.3-5.2)	0.1% [21/14,102] (0.1-0.2)	0.7% [18/2,470] (0.4-1.1)
CT brain imaging within 2 days of procedure	8.1% [89/1,101] (6.5-9.7)	7.1% [16/224] (4.0-10.7)	2.1% [207/10,039] (1.8-2.3)	3.2% [71/2,187] (2.5-4.0)
LOS more than 2 days	57.0% [628/1,101] (54.1-60.0)	64.3% [144/224] (58.0-70.5)	28.5% [2,864/10,039] (27.7-29.4)	27.5% [601/2,187] (25.6-29.4)

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; CI: Confidence Interval; CT: Computerised Tomography; LOS – Length of Stay.

Discussion

Our study has demonstrated, in a large administrative dataset of recent practice, that death, post-procedural CT brain imaging rate (proxy for suspected stroke) and prolonged LOS following carotid intervention were observed more frequently in symptomatic than asymptomatic patients. Symptomatic patients undergoing CAS had an increased risk of death, possibly due to selection bias. Procedural risks reported in this study might be more generalisable than RCT findings. Whilst RCTs robustly compare long-term efficacy of CEA and CAS, administrative data can reliably estimate contemporary procedural outcomes.

CEA Outcomes: Symptomatic patients (Table 5.3)

Mortality following CEA in symptomatic patients was 0.2% in our study. This is broadly consistent with findings from other RCTs that have examined CEA outcomes in symptomatic patients. CREST-1[6, 7] reported no deaths following CEA in a small subgroup of symptomatic patients. However, older RCTs reported higher mortality than our study. CAVATAS[1], EVA-3S[8], SPACE-1[9] and ICSS[10] reported mortality rates of 1.6%, 1.2%, 0.9% and 0.5% respectively following CEA in symptomatic patients. This suggests temporal improvement in outcomes, possibly due to increased sophistication of operative techniques, improved CMT, technological advancement and more refined patient selection.

Suspected stroke rate following CEA in symptomatic patients was 8.1% in our study. This is similar to the stroke rate reported in CAVATAS[1] (8.3%) and SPACE-1[9] (6.2%) but higher than in CREST-1[7] (3.2%), EVA-3S[8] (2.7%) and ICSS[10] (3.3%). This may be due to our outcome measure over-estimating stroke rate following CEA, especially in symptomatic patients, due to their smaller sample size and some patients having CT brain imaging but no procedural stroke.

CEA Outcomes: Asymptomatic patients (Table 5.4)

Mortality following CEA in asymptomatic patients was 0.1% in our study, which is broadly consistent with RCT findings. Whilst CREST-1[7] and SPACE-2[11] reported no deaths following CEA in asymptomatic patients, their cohort of patients were smaller than our study and their outcomes had wide CIs, suggesting a need to interpret their results with caution. Our results have greater power in estimating mortality following CEA in asymptomatic patients and are similar to the 0.3% mortality described in ACT-1.[12]

Suspected stroke rate following CEA in asymptomatic patients was 2.1% in our study. This is comparable to the stroke rate following CEA reported in CREST-1[7] (1.4%), ACT-1[12] (1.4%) and SPACE-2[11] (2.0%). As our results are comparable to findings from the largest RCT performed in this area (CREST-1[7]) and RCTs that reported their results in the last few years (SPACE-2[11] and ACT-1[12]), this supports the reliability of our data, suggesting that administrative data accurately reflect contemporaneous practice.

CAS Outcomes: Symptomatic patients (Table 5.3)

Mortality following CAS in symptomatic patients was 3.3% in our study. This is broadly consistent with CAVATAS[1] (2.8%). However, reported mortality in our study following CAS in symptomatic patients was higher than in CREST-1[7] (0.4%), EVA-3S[8] (0.8%), SPACE-1[9] (0.7%) and ICSS[10] (1.3%). This may be explained by case selection, with more co-morbid patients preferentially undergoing CAS in our study (IHD was significantly more common in CAS than CEA patients). This selection bias would have been minimised by randomisation in RCTs. Our high mortality following CAS in symptomatic patients may also be explained by the smaller number of symptomatic patients undergoing CAS in our dataset. This trend for excess mortality following CAS in symptomatic patients is consistent with RCT findings and

supported by a systematic review that reported procedural risks of stroke/death following CAS in symptomatic patients exceeding 10% in 28% of reports from registries.[13]

Suspected stroke rate following CAS in symptomatic patients was 7.1% in our study. This is similar to the stroke rate following CAS reported in RCTs. CAVATAS[1], CREST-1[7] EVA-3S[8], SPACE-1[9] and ICSS[10] reported stroke rates of 7.2%, 5.5%, 8.8%, 7.5% and 7.0% respectively. Our findings are consistent with those from RCTs, suggesting that analyses of administrative data may be a useful adjunct in assessing procedural outcomes.

CAS Outcomes: Asymptomatic patients (Table 5.4)

Mortality following CAS in asymptomatic patients was 0.7% in our study. This is broadly consistent with mortality reported in ACT-1[12] (0.1%). Both CREST-1[7] and SPACE-2[11] reported no deaths following CAS in asymptomatic patients but, due to the small number of patients analysed, their results should be interpreted with caution. There is a paucity of data available on CAS procedural outcomes in asymptomatic patients, but our results suggest that administrative data analyses can provide similar findings to RCTs.

Suspected stroke rate following CAS in asymptomatic patients was 3.2% in our study. This is similar to the stroke rate reported in CREST-1[7] (2.5%), SPACE-2[11] (2.5%) and ACT-1[12] (2.8%), again suggesting that administrative data may reliably estimate procedural risks.

Table 5.3: Comparison of procedural death and stroke rates following CEA and CAS in symptomatic patients, reported in the Global Comparators' dataset and various randomised clinical trials. CT brain imaging rate was used as a proxy measure for suspected or actual procedural stroke in the Global Comparators' dataset.

	Mortality Rate (%)		**CT brain imaging/Stroke Rate (%)**	
	CEA	**CAS**	**CEA**	**CAS**
GC data	**0.2**	**3.3**	**8.1**	**7.1**
EVA-3S	1.2	0.8	2.7	8.8
SPACE-1	0.9	0.7	6.2	7.5
ICSS	0.5	1.3	3.3	7.0
CAVATAS	1.6	2.8	8.3	7.2
CREST-1	0.0	0.4	3.2	5.5

Abbreviations – CAS: Carotid Artery Stenting; CAVATAS: Carotid and Vertebral Artery Transluminal Angioplasty Study; CEA: Carotid Endarterectomy; CREST: Carotid Revascularisation Endarterectomy versus Stenting Trial; CT: Computerised Tomography; EVA-3S: Endarterectomy Versus Stenting in patients with Symptomatic Severe Carotid Stenosis; GC: Global Comparators'; ICSS: International Carotid Stenting Study; SPACE: Stent-Protected Angioplasty versus Carotid Endarterectomy.

Table 5.4: Comparison of procedural death and stroke rates following CEA and CAS in asymptomatic patients, reported in the Global Comparators' dataset and various randomised clinical trials. CT brain imaging rate was used as a proxy measure for suspected or actual procedural stroke in the Global Comparators' dataset.

	Mortality Rate (%)		**CT brain imaging/Stroke Rate (%)**	
	CEA	**CAS**	**CEA**	**CAS**
GC data	**0.1**	**0.7**	**2.1**	**3.2**
CREST-1	0.0	0.0	1.4	2.5
ACT-1	0.3	0.1	1.4	2.8
SPACE-2	0.0	0.0	2.0	2.5

Abbreviations – ACT: Asymptomatic Carotid Stenosis; CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; CT: Computerised Tomography; CREST: Carotid Revascularisation Endarterectomy versus Stenting Trial; SPACE: Stent-Protected Angioplasty versus Carotid Endarterectomy.

Prolonged LOS

Prolonged LOS is rarely used as an outcome following carotid intervention.[5] In an American registry study, McPhee *et al*.[14] reported a longer LOS for symptomatic patients undergoing carotid intervention compared to asymptomatic patients. For asymptomatic patients, they also reported similar LOSs following CEA and CAS.[14] This is broadly consistent with our findings (Table 5.2) and suggest that prolonged LOS may be a useful proxy measure for suspected or actual procedural complications following carotid intervention.[5]

Strengths

The GC database captured a large number of CEAs (but fewer CAS procedures). The 28 contributing centres were from 7 countries, representing practice globally, with high-quality data provided for analysis. Remuneration was linked to the number of patients entered into each contributing centre's database, limiting the number excluded from the GC dataset. Procedures were also performed between 2011-2015, representing recent practice.

Limitations

GC centres were technologically advanced, academic and interested in quality improvement so their practice may not be representative of all centres. There may have also been selection bias with more co-morbid patients undergoing CAS (whose sample size was limited).

The database did not capture events beyond 7 days post-procedure or outside hospital whilst our proxy measure may have over-estimated procedural strokes in symptomatic patients undergoing CEA, possibly due to their smaller number and some patients having CT brain imaging but no stroke. Self-reporting of complications may have also introduced bias.

Conclusions and Implications

Our study has demonstrated, in a large recent administrative dataset, that death, CT brain imaging rate (proxy for suspected procedural stroke) and prolonged LOS following carotid intervention were more commonly associated with symptomatic than asymptomatic patients. Observed rates of procedural death were particularly high in symptomatic patients undergoing CAS. This may be partly explained by case selection, where more co-morbid patients preferentially underwent CAS. Procedural risks reported in this study may be more generalisable than RCT findings. Whilst RCTs robustly compare long-term efficacy of CEA and CAS, administrative data can reliably estimate contemporary procedural outcomes.

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CHAPTER 6: Temporal and Regional Trends in the Provision of Carotid Interventions in England between 2001-2016

Abstract

Background: It is unknown how age-standardised CEA and CAS rates have changed since the first RCT comparing them was published in 2001. There is also a paucity of data reporting regional differences in the provision of carotid interventions. This study aimed to describe temporal and regional trends in CEA and CAS provision in England.

Methods: Patients receiving CEA or CAS between 2001-2016 were identified in the Hospital Episode Statistics (HES) dataset using Office of Population Censuses and Surveys Classification of Interventions and Procedures version 4 codes. Procedures were divided into 8 separate year groups and 9 regions. Age-standardised CEA and CAS rates were calculated using corresponding Office for National Statistics population statistics. Cohorts were compared statistically using Chi-squared and Mann-Whitney U tests.

Results: Overall, 68,897 carotid procedures were analysed, with the majority (96.2%) being CEA (n=66,267). The age-standardised CEA rate increased from 2001-2002 until its peak in 2011-2012 (21.0 per 100,000 population), before a 25% reduction by 2015-2016. The age-standardised CAS rate increased from 2001-2002 until its peak in 2007-2008 (0.9 per 100,000 population), before a 22% reduction in 2009-2010 and a gradual decline thereafter. Patients undergoing CEA were significantly more likely to be older, affluent, White ethnicity, symptomatic and hypertensive whereas CAS patients were significantly more likely to suffer from congestive heart failure (CHF), ischaemic heart disease (IHD) and peripheral vascular disease (PVD). The North West and North East performed CEA and CAS most commonly whereas the South East had one of the lowest CEA and CAS rates.

Conclusions: This 16-year analysis of CEA and CAS provision has shown that CEA is more common than CAS but there has been a reduction in both procedures since 2011-2012 with regional variation in provision. Further investigation is required to understand reasons for these findings which may inform future configuration of vascular services in England.

Introduction

This chapter will analyse the HES dataset over a 16 year period to describe temporal and regional trends in CEA and CAS provision in England, overcoming some of the challenges presented in the previous chapter when analysing large administrative datasets.

HES data: Background

Data are collected on all patients admitted to NHS hospitals in England. A hospital admission is defined as "any secondary care-based activity that requires a hospital bed", including emergency and elective admissions.[1] Each hospital admission is termed a 'spell' and comprises periods of care under one or more Consultants, known as 'Finished Consultant Episodes' (FCEs).[1] FCEs have start and end dates when the patient is transferred under the care of another Consultant. If a patient is transferred to another hospital, a new spell begins but they are grouped together as 'Continuous Inpatient Spells'.[1] This allows a patient's journey to be constructed and aspects analysed in detail. In 2017-2018, 20 million FCEs were recorded in the HES dataset.[2]

Each patient's discharge summary is sent to the Clinical Coding Department in the hospital. Data relating to demographics, dates of admission and discharge, diagnoses and procedures are entered on the local electronic patient information database.[1] Other details such as regional variables, ethnicity and degree of affluence/deprivation (estimated by the Index of Multiple Deprivation (IMD) score) are also recorded.[1] Clinical coders follow standardised rules for converting data from discharge summaries into codes. Diagnoses are recorded using ICD-10 codes.[1] Each FCE has one primary diagnosis (main reason for admission) and other comorbidities recorded.[1] Interventions (including operations) are coded using the Office of

Population Censuses and Surveys Classification of Interventions and Procedures version 4 (OPCS-4) codes.[1] A primary procedure is coded for each FCE with a corresponding date.[1] Recording of data is incentivised by the 'Payment by Results' system that has been applied since 2003-2004 with 270 variables able to be recorded per patient. This reimburses hospitals every month commensurate with the amount of activity that has been undertaken.

Each month, data are extracted from local databases and inputted into the Secondary User Service – a data warehouse within NHS Digital.[1] These data are used to create the monthly HES dataset.[1] This is checked, processed, cleaned and each patient is assigned a unique HES identification (HESID) number for linkage of all admissions.[1] The HES dataset is also linked to the Office for National Statistics' (ONS) Register of Deaths in England and Wales.[1] This allows all deaths to be captured for patients in the HES dataset (since 1998). Each monthly datasheet is combined and an annual extract produced for the end of the Financial Year (as the primary purpose of HES data is reimbursement of hospitals).[1]

HES data: Strengths

The long period of data collection and linkage of episodes to individual patients allows population-level analyses to increasingly be conducted using the HES dataset. In 2013, a systematic review reported 148 studies using HES data between January 1989 – July 2011.[3] However, between July 2011 – June 2016, 264 studies used HES as their primary data source, with 130 further studies using other datasets linked to HES.[1] The annual number of publications using HES data increased from 2 in 1993 to 88 in 2015.[3] HES data provide an unselected sample of patients, reflecting current practice. The large sample size also provides power to estimate complication rates that may be low.

A further strength of HES data is its ability to link admissions to a single patient using the HESID. This allows construction of a patient pathway in a large cohort of patients who can be followed for a number of years. As HES data are also linked to ONS death records, this may provide information about the natural history of certain diseases and their prognosis. Linkage to care costs also allows economic comparisons relating to the use of healthcare services.[1]

Standardised coding of diagnoses and interventions using ICD-10 and OPCS-4 codes respectively allows precise definition of patient populations within the HES dataset. It also allows international comparisons of secondary care use in Europe, Canada, Australia and New Zealand as these countries use similar coding systems.[1] However, these are limited by confounders such as differences in organisation of healthcare and whether it is free at the point of use or requires insurance. HES data also have other limitations.

HES data: Limitations

HES data accuracy is dependent on clinical coders reliably converting data from discharge summaries into diagnostic and procedure codes. This relies on the accuracy of information in the discharge summary and consistency of coding practices nationally. These are challenges despite centrally issued coding rules and a requirement for coders to undergo nationally accredited training programmes.[1]

Coding accuracy in the early years of the HES dataset may be less than in later years. A systematic review reported that overall coding accuracy improved from 77.0% to 86.1% after 2004 following the introduction of the Payment by Results system.[4] Coding accuracy of the primary diagnosis significantly increased from 73.8% to 96.0% ($p=0.02$).[4] This is likely due to reimbursement incentives for accurate coding and may explain the increase in the number of

codes used. This limitation needs to be considered when analysing temporal trends over a long period using the HES dataset.

HES data only include admitted patients and reflect variations in admission thresholds over time between hospitals. No information is provided for interventions undertaken on patients admitted to HDU or ICU and HES data do not include outpatients or patients treated in the community.[1] Therefore, there is potential for bias from retrospective analyses that generalise findings to all patient populations. Medications prescribed during the hospital stay are also not included and data regarding ethnicity are not well recorded, with only 41% recorded in 1997.[5] However, this has improved over time with 85% having ethnicity recorded in 2011.[5]

There is also a 4% HESID 'missed match' rate where FCEs have failed to be linked to a single patient due to errors with recording patients' NHS numbers in their discharge summaries.[1] A patient may also request that their hospital records are not exported into the HES dataset. This is via the 'national data opt-out' system. By January 2019, over 1.5 million patients had chosen not to share their health data, accounting for 2.75% of episodes.[6]

Rationale for Study

Various North American studies have used Centers for Medicare and Medicaid Services (CMS) and NIS datasets to describe temporal reductions in rates of carotid intervention.[7-18] American Heart Association statistics also support the above studies, reporting a significant decline in the annual number of CEAs performed from 154,000 in 1997 to 88,000 in 2013.[19] Between 2001-2010, the carotid revascularisation rate fell from 740 to 490 per million adults (a 34% reduction in CEAs performed).[19] This decrease in CEA rates in North America was accompanied by an increase in CAS provision.[7-17]

In the UK, a recent study[20] (whose results were not age-standardised) reported a 30% decline in CEA provision since 2013 in 29,875 patients recorded in the NVR between 2011-2017. In symptomatic patients (86% of the cohort), there was a 25% relative reduction in CEAs performed whilst in asymptomatic patients (14% of the cohort), there was a 63% relative decline.[20] However, this study was limited by the fact that CAS provision was not reported and the period of analysis was short. CEA provision was also expressed as a function of stroke admissions. This is a major limitation as stroke admissions are not an accurate measure of demand for CEA. There is also variable quality of coding for cerebrovascular disease in the HES dataset and outpatient encounters (e.g. TIA diagnoses) were not captured. Moreover, annual variation in the numbers of stroke diagnoses in the period analysed may artificially affect CEA rate whilst major confounders (e.g. age) were not corrected.

CAS provision is different in the UK compared to North America. An English study[21], conducted between 2009-2012 in patients undergoing CEA (n=15,996) and CAS (n=632) in HES data, reported that CAS accounted for less than 5% of all carotid interventions each year. The number of CEAs increased between 2006 to 2009 whilst CAS procedures peaked at 70 in quarter 3 of 2008 and remained static since.[21] This may reflect a more conservative approach in CAS use in England compared to the USA and Canada, which may be due to worse procedural outcomes following CAS than CEA in English practice.[21]

Data relating to regional trends in CEA and CAS provision are sparse, with only a few studies conducted in the USA[8, 9], Canada[22] and UK.[23-25] In a recent study, Johal *et al*.[20] reported variation between 9 English regions in the number of CEAs performed between 2011-2017. Activity in the North West and South East decreased substantially whilst smaller reductions occurred in the East Midlands, London, South West and West Midlands.[20] However, there were no changes in activity in the North East, East of England or Yorkshire and the Humber.[20]

Therefore, there is a need to examine temporal and regional trends in CEA and CAS provision in England in more detail as the few studies conducted have assessed a short time period and there is a paucity of data describing regional trends in CEA and CAS provision. Major confounders for CEA and CAS provision (e.g. age) have also not been adjusted in analyses.

Aim

This study aimed to use HES data to describe age-standardised temporal and regional trends in CEA and CAS provision in England between 2001-2016.

Methods

HES data are held by the Unit of Healthcare Epidemiology at the Big Data Institute, University of Oxford. Approval was granted for access to the HES dataset and ONS accreditation was also obtained before accessing data. Support with data cleaning was provided by Charlie Harper.

Study Population

All adult patients (aged 18 years or over) undergoing CEA or CAS between January 2001 and December 2016 (inclusive) were included in this cross-sectional analysis. Primary procedures were identified using the relevant OPCS-4 codes, detailed below (Table 6.1).

Table 6.1: OPCS-4 codes defining CEA and CAS in the HES dataset.

OPCS-4 Code	Description
L29.4	Endarterectomy of carotid artery and patch repair of carotid artery
L29.5	Endarterectomy of carotid artery NEC
L31.1	Percutaneous transluminal angioplasty of carotid artery
L31.4	Percutaneous transluminal insertion of stent into carotid artery

Abbreviations – NEC: Not Elsewhere Classified; OPCS: Office of Population Censuses and Surveys Classification of Interventions and Procedures.

Cohort Characteristics

Baseline information of all patients was obtained from the HES dataset, including date of birth, age, gender, IMD score (marker of degree of affluence/deprivation) and ethnicity ('White', 'Black', 'South Asian' or 'Chinese' as reported in HES). Date and type of procedure (CEA or CAS), LOS and discharge destination (usual place of residence; NHS ward; NHS care home; residential accommodation; non-NHS care home; non-NHS hospital; non-NHS hospice; other) was recorded, along with if the patient died, experienced a stroke or was re-admitted to hospital within 30 days of the procedure.

Comorbidities were also recorded if a diagnosis was entered in the HES dataset up to 2 years before the patient underwent CEA or CAS. Table 6.2 lists all ICD-10 codes used.

Patients were classed as 'symptomatic' if their discharge diagnosis contained any of the ICD-10 codes listed in Table 6.3, in the 6 months prior to CEA or CAS. Specifically, ischaemic stroke was diagnosed if the discharge diagnosis contained codes I63 and/or I64, TIA was diagnosed if the discharge diagnosis contained codes G45.1 and/or G45.3 and/or G45.8 and/or G45.9 and a patient was deemed 'ever symptomatic' if the discharge diagnosis contained codes G46.0 and/or G46.1 and/or G46.2 and/or H34 and/or I65.2 and/or I65.3 and/or I66. The latter category included contralateral symptoms and ill-defined diagnoses of ischaemic events.

Table 6.2: ICD-10 codes defining comorbidities in the HES dataset.

Comorbidity	ICD-10 Code	Description
DM	E10	Insulin-dependent diabetes mellitus
	E11	Non-insulin-dependent diabetes mellitus
	E12	Malnutrition-related diabetes mellitus
	E13	Other specified diabetes mellitus
	E14	Unspecified diabetes mellitus
HTN	I10	Essential (primary) hypertension
	I11	Hypertensive heart disease
	I12	Hypertensive renal disease
	I13	Hypertensive heart and renal disease
	I15	Secondary hypertension
IHD	I20	Angina pectoris
	I21	Acute myocardial infarction
	I22	Subsequent myocardial infarction
	I23	Certain current complication post-acute myocardial infarction
	I24	Other acute ischaemic heart diseases
	I25	Chronic ischaemic heart disease
CHF	I50	Heart failure
PVD	I70.2	Atherosclerosis of arteries of extremities
	I73.9	Peripheral vascular disease, unspecified
	Z95.8	Presence of other cardiac and vascular implants and grafts
CRF	N18	Chronic kidney disease
	N19	Unspecified kidney failure

Abbreviations – CRF: Chronic Renal Failure; CHF: Congestive Heart Failure; DM: Diabetes Mellitus; HTN: Hypertension; ICD: International Classification of Diseases; IHD: Ischaemic Heart Disease; PVD: Peripheral Vascular Disease.

Table 6.3: ICD-10 codes defining symptom status in the HES dataset.

ICD-10 Code	Description
G45.1	Carotid artery syndrome
G45.3	Amaurosis fugax
G45.8	Other transient cerebral ischaemic attacks and related syndromes
G45.9	Transient cerebral ischaemic attack, unspecified
G46.0	Middle cerebral artery syndrome
G46.1	Anterior cerebral artery syndrome
G46.2	Posterior cerebral artery syndrome
H34	Retinal vascular occlusions
I63	Cerebral infarction
I64	Stroke not specified as haemorrhage or infarction
I65.2	Occlusion and stenosis of carotid artery
I65.3	Occlusion and stenosis of multiple and bilateral precerebral arteries
I66	Occlusion and stenosis of cerebral arteries, not resulting in infarction

Abbreviation – ICD: International Classification of Diseases.

Temporal Trends

Temporal trends in CEA and CAS provision were assessed by categorising the number of procedures into 8 groups: 2001-2002; 2003-2004; 2005-2006; 2007-2008; 2009-2010; 2011-2012; 2013-2014; 2015-2016. These were further stratified by age (18-39; 40-49; 50-59; 60-69; 70-79; and ≥80 years) for each 2-year group.

ONS data were used to obtain an estimate of the corresponding number of individuals of the general, underlying population in each age category for each 2-year group.[26] The rate of CEA or CAS was calculated for each age category per 2-year group (by dividing the number of procedures in each age category by the corresponding number of individuals of the general, underlying population). An unweighted average of the rates across all age categories was calculated to obtain the age-standardised CEA or CAS rate for each 2-year group. This was expressed per 100,000 population.

Regional Trends

The region in which CEA or CAS was performed was defined using the Government Office Region of Residence (RESGOR) variable provided in the HES dataset. RESGOR divided England into 9 regions: North East; North West; Yorkshire and Humber; East Midlands; West Midlands; East of England; London; South East; and South West.

The total number of CEA and CAS procedures performed in each region between 2001-2016 was divided by the total number of corresponding individuals of the general, underlying population (aged ≥18 years) recorded as living in that region between 2001-2016, according to ONS population statistics.[26] This allowed a rate to be expressed per 100,000 population.

Study Outcomes

The primary outcome was the age-standardised rate of CEA and CAS procedures performed in England between 2001-2016 (expressed per 100,000 population). Secondary outcomes included regional rates of CEA and CAS provision (expressed per 100,000 population) and description of baseline cohort characteristics.

Statistics

Cohort characteristics were compared statistically using the Chi-squared test, except for median age and median LOS where the Mann-Whitney U test was used.

A p-value ≤ 0.05 was deemed statistically significant. All analyses were performed using Stata, version 15.1 (StataCorp LLC, Texas, USA).

Results

Overall, 68,897 CEA and CAS procedures were performed in England between January 2001 and December 2016 (Table 6.4), with the majority (96.2%) being CEA (n=66,267). Patients undergoing CEA tended to be significantly older than those undergoing CAS, with CAS being significantly more frequently used in patients under the age of 70 years whilst CEA was significantly more common in patients aged 70 years and above (Table 6.4). There was no gender difference in patients undergoing CEA or CAS (Table 6.4).

The North West region had the highest number of patients receiving carotid interventions whilst the North East had fewest number of patients receiving carotid interventions (Table 6.5). A similar trend existed for the numbers of CEA performed. However, for CAS, Yorkshire and the Humber performed the most and the South West performed the least (Table 6.5).

Table 6.4: Overall characteristics of patients undergoing CEA and CAS in the HES dataset between 2001-2016.

Characteristic	CEA	CAS	p-value	TOTAL
Procedures (n)	66,267	2,630		**68,897**
Median Age (IQR)	72.4 (65.5-78.4)	69.1 (61.1-75.8)	**<0.00001**	
Patient Age				
18-39 (n, %)	71 (0.1)	61 (2.3)	**<0.0001**	
40-49 (n, %)	1,081 (1.6)	141 (5.4)	**<0.0001**	
50-59 (n, %)	6,852 (10.3)	373 (14.2)	**<0.0001**	
60-69 (n, %)	18,877 (28.5)	822 (31.4)	**0.002**	
70-79 (n, %)	26,593 (40.2)	878 (33.5)	**<0.0001**	
≥80 (n, %)	12,736 (19.2)	346 (13.2)	**<0.0001**	
TOTAL	**66,210**	**2,621**		**68,831**
Percentage male	67.3% (44,610/66,263)	65.6% (1,726/2,630)	0.069	**68,893**

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; IQR: Inter-Quartile Range.

Table 6.5: Crude total number of patients undergoing CEA and CAS, by region, in the HES dataset between 2001-2016.

Region	CEA	CAS	TOTAL
North East (n, %)	3,853 (93.4)	272 (6.6)	**4,125**
North West (n, %)	11,894 (96.6)	425 (3.4)	**12,319**
Yorkshire and Humber (n, %)	7,133 (92.2)	606 (7.8)	**7,739**
East Midlands (n, %)	5,195 (95.9)	220 (4.1)	**5,415**
West Midlands (n, %)	7,555 (98.1)	144 (1.9)	**7,699**
East of England (n, %)	6,697 (96.9)	216 (3.1)	**6,913**
London (n, %)	5,976 (95.2)	302 (4.8)	**6,278**
South East (n, %)	9,567 (97.3)	269 (2.7)	**9,836**
South West (n, %)	7,780 (98.5)	121 (1.5)	**7,901**
TOTAL	**65,650**	**2,575**	**68,225**

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy.

Cohort Characteristics

Patients undergoing CEA were significantly more likely to be from the highest quintiles of affluence whereas CAS was significantly more common in patients from the highest quintile of deprivation (Table 6.6). The majority of patients undergoing both CEA and CAS were White ethnicity, with CAS significantly more common in ethnic minorities (Table 6.7).

Patients undergoing CEA were significantly more likely to have been symptomatic in the past (including contralateral symptoms) and suffer from HTN than patients receiving CAS (Table 6.8). Patients undergoing CAS were significantly more likely to suffer from CHF, IHD and PVD than patients receiving CEA but rates of DM and CRF were comparable between CEA and CAS cohorts (Table 6.8).

Table 6.6: Degree of affluence/deprivation of patients undergoing CEA and CAS in the HES dataset between 2001-2016.

IMD score	CEA	CAS	p-value	TOTAL
Quintile 1 (n, %)	13,292 (20.2)	455 (17.5)	**0.001**	13,747
Quintile 2 (n, %)	13,258 (20.1)	443 (17.1)	**<0.0001**	13,701
Quintile 3 (n, %)	13,212 (20.0)	488 (18.8)	0.126	13,700
Quintile 4 (n, %)	13,168 (20.0)	531 (20.5)	0.533	13,699
Quintile 5 (n, %)	13,031 (19.8)	678 (26.1)	**<0.0001**	13,709
TOTAL	65,961	2,595		**68,556**

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; IMD: Index of Multiple Deprivation.

Table 6.7: Ethnicity of patients undergoing CEA and CAS in the HES dataset between 2001-2016.

Ethnicity	CEA	CAS	p-value	TOTAL
White (n, %)	60,480 (96.0)	2,377 (94.6)	**<0.0001**	62,857
Black (n, %)	330 (0.5)	30 (1.2)	**<0.0001**	360
South Asian (n, %)	1,298 (2.1)	50 (2.0)	0.807	1,348
Chinese (n, %)	33 (0.1)	6 (0.2)	**<0.0001**	39
Other (n, %)	836 (1.3)	49 (2.0)	**0.008**	885
TOTAL	62,977	2,512		**65,489**

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy.

Table 6.8: Comorbidities of patients undergoing CEA and CAS in the HES dataset between 2001-2016.

Comorbidity	CEA (n=66,267)	CAS (n=2,630)	p-value
Stroke (n, %)	17,770 (26.8)	750 (28.5)	0.054
TIA (n, %)	13,856 (20.9)	553 (21.0)	0.885
Ever symptomatic (n, %)	34,018 (51.3)	1,217 (46.3)	**<0.0001**
CHF (n, %)	2,865 (4.3)	196 (7.5)	**<0.0001**
IHD (n, %)	20,312 (30.7)	1,011 (38.4)	**<0.0001**
HTN (n, %)	44,997 (67.9)	1,717 (65.3)	**0.005**
PVD (n, %)	7,253 (10.9)	440 (16.7)	**<0.0001**
DM (n, %)	14,137 (21.3)	585 (22.2)	0.264
CRF (n, %)	3,305 (5.0)	150 (5.7)	0.099

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; CHF: Congestive Heart Failure; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; IHD: Ischaemic Heart Disease; HTN: Hypertension; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

CEA and CAS Provision: Temporal Trends

The CEA rate increased from 2001-2002 until its peak (21.0 per 100,000 population) in 2011-2012 (Figure 6.1 (a)). This was followed by a greater than 25% reduction until 2015-2016 (15.7 per 100,000 population), which is the same CEA rate as in 2003-2004 (Figure 6.1 (a)).

The CAS rate increased from 2001-2002 until its peak (0.9 per 100,000 population) in 2007-2008 (Figure 6.1 (b)). This was followed by a greater than 20% reduction in 2009-2010 (0.7 per 100,000 population), after which the CAS rate has gradually declined (Figure 6.1 (b)).

Overall, CAS accounted for 3.8% of all carotid interventions. However, as a proportion of CEA, it peaked in 2007-2008 (5.0%) before dropping to 3.7% in 2008-2009. Since then, it has gradually increased to 4.8% in 2015-2016.

CEA and CAS Provision: Regional Trends

The North West and North East performed CEA and CAS most commonly whereas the South East had one of the lowest rates of CEA and CAS per 100,000 population (Figures 6.2 and 6.3). The North West had the highest CEA rate per 100,000 population whilst London had the lowest (Figure 6.2). Yorkshire and the Humber had the highest CAS rate per 100,000 population whilst the South West had the lowest (Figure 6.3). Although the South West had the lowest CAS rate per 100,000 population, it had one of the highest CEA rates, similar to the West Midlands.

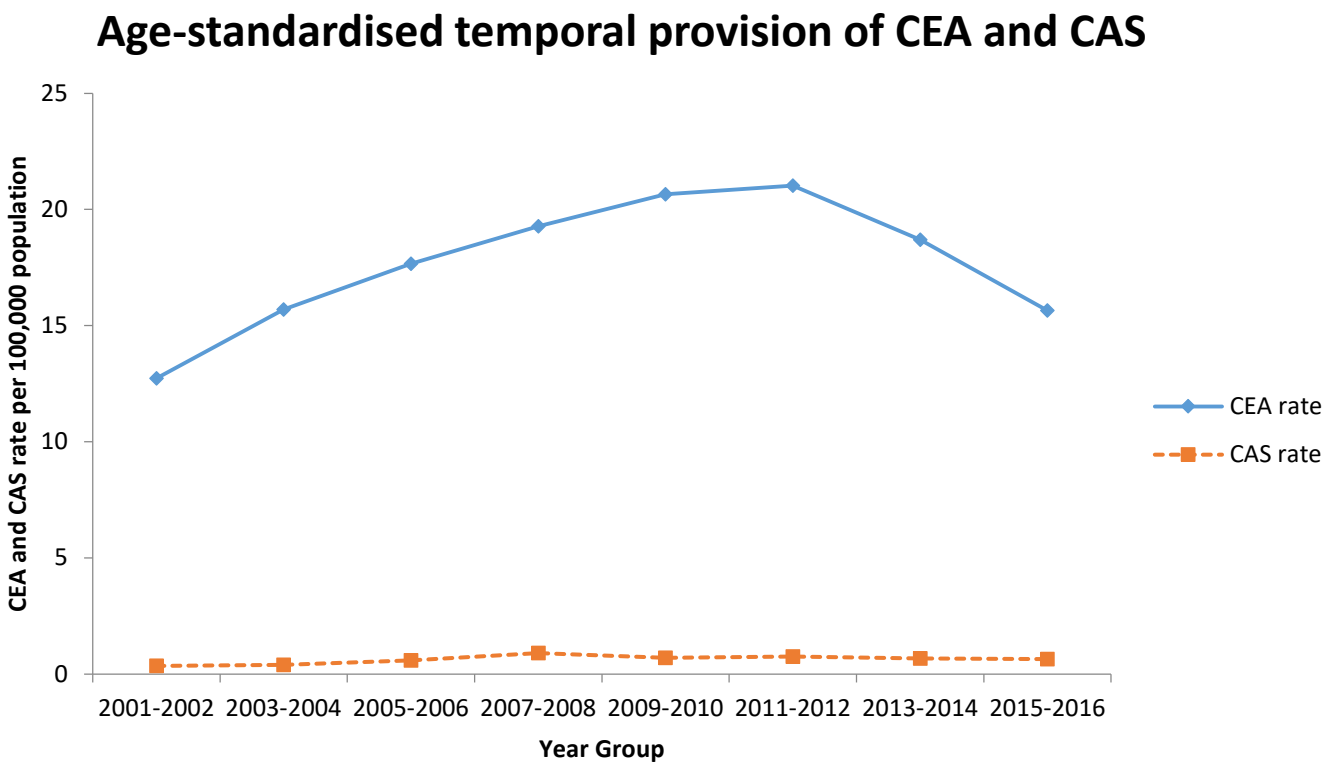

Figure 6.1 (a): Age-standardised CEA and CAS rates per 100,000 population in England between 2001-2016.

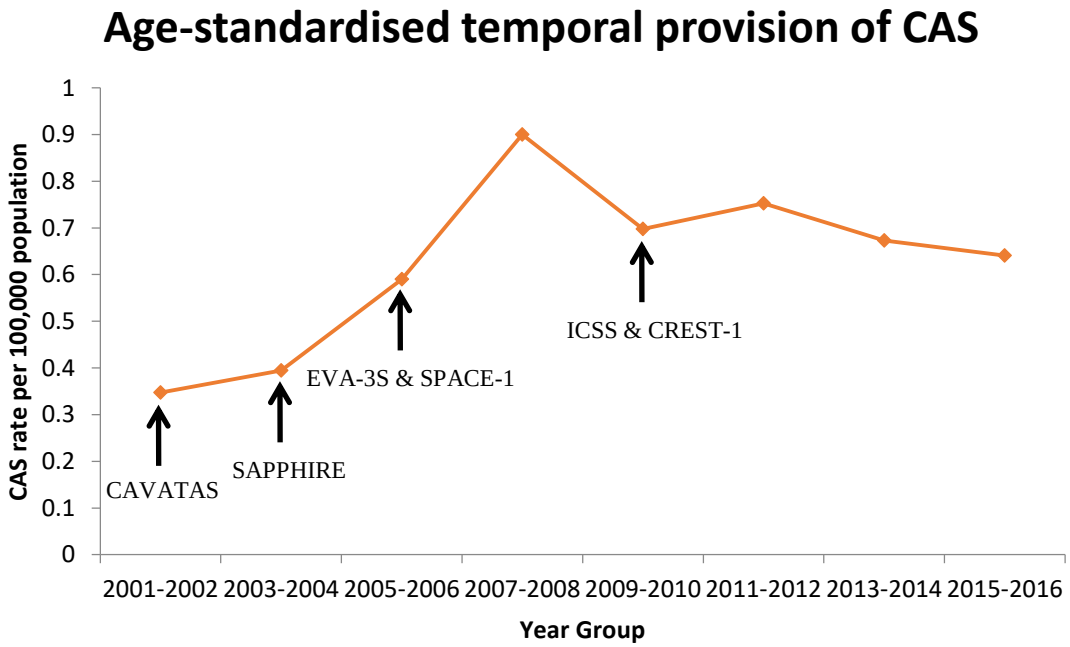

Figure 6.1 (b): Age-standardised CAS rate per 100,000 population in England between 2001-2016. Annotations show when various RCTs comparing CEA versus CAS were published.

Region	CEA rate per 100,000
North West	13.68
North East	11.79
South West	11.71
West Midlands	11.08
Yorkshire and Humber	10.92
East of England	9.32
East Midlands	9.28
South East	9.03
London	6.06

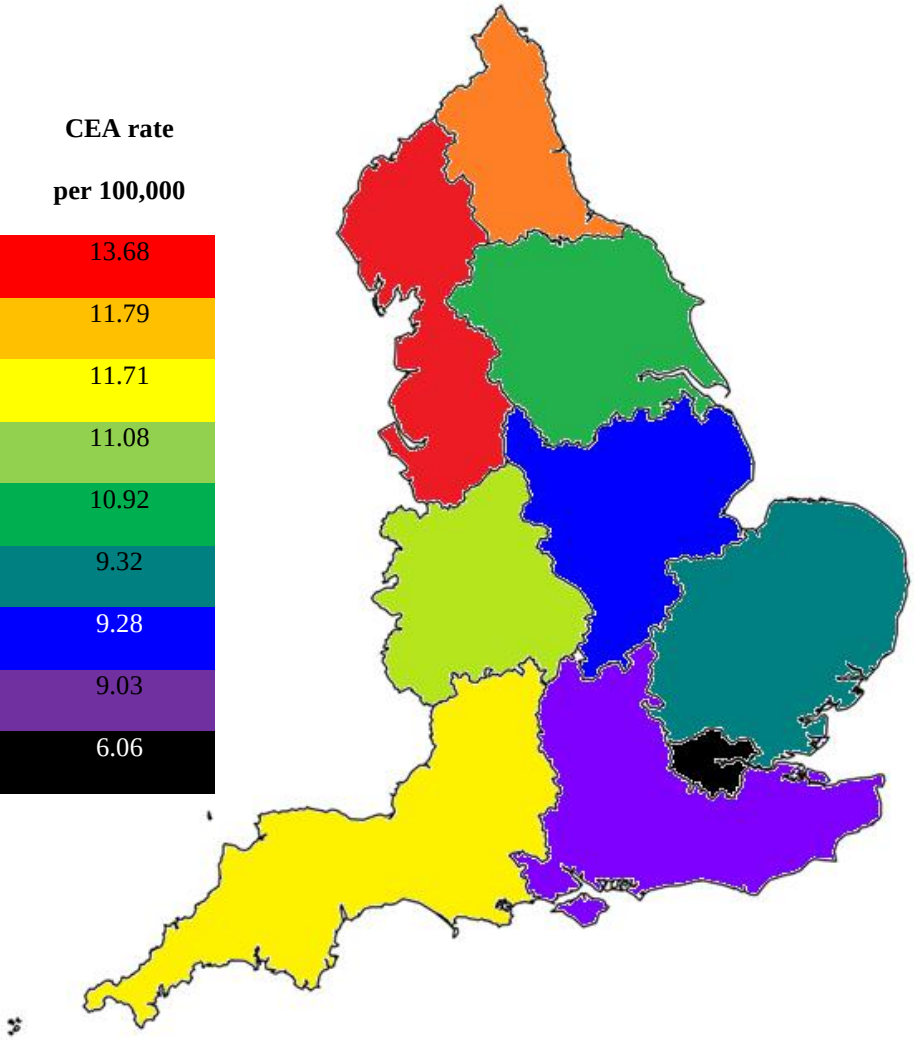

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Figure 6.2: Regional CEA rate per 100,000 population in England between 2001-2016.

Region	CAS rate per 100,000
Yorkshire and Humber	0.93
North East	0.83
North West	0.49
East Midlands	0.39
London	0.31
East of England	0.30
South East	0.25
West Midlands	0.21
South West	0.18

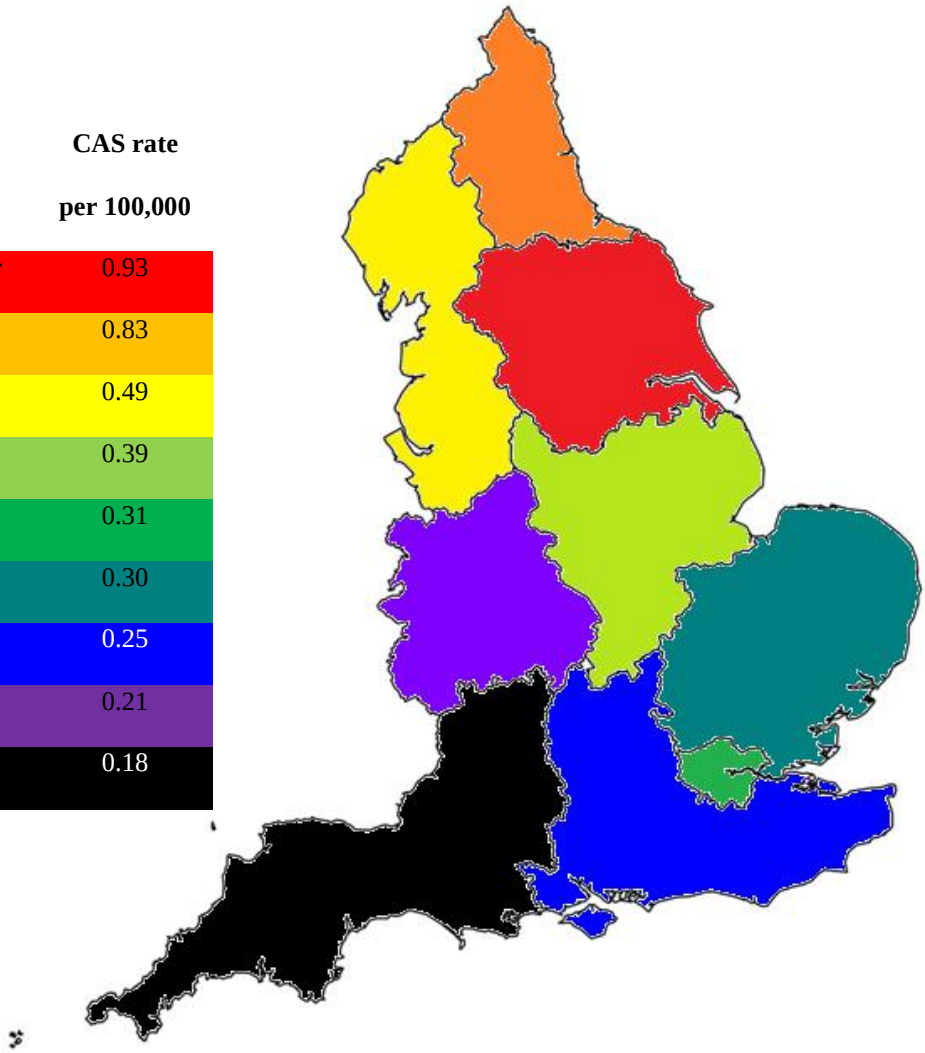

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Figure 6.3: Regional CAS rate per 100,000 population in England between 2001-2016.

Discussion

This 16-year analysis of 68,897 patients undergoing carotid interventions in the HES dataset has shown that there has been a greater than 25% reduction in the age-standardised CEA rate since 2011-2012. There has also been a greater than 20% reduction in the age-standardised CAS rate since 2009-2010. Whilst CEA was more common than CAS overall, older, affluent, White patients were significantly more likely to receive CEA than CAS but patients with CHF, IHD and PVD were significantly more likely to undergo CAS than CEA. Regional variation also existed in the provision of carotid interventions with the North West and North East performing CEA and CAS most commonly whilst the South East had one of the lowest rates of both CEA and CAS per 100,000 population. This is the first age-standardised temporal and regional analysis of CEA and CAS provision in England over 16 years. Further investigation of this study's findings may inform future configuration of vascular services.

Trends in Provision: Patient Characteristics

Our finding that patients receiving CAS were significantly more likely to suffer from IHD and cardiac comorbidities than patients undergoing CEA is supported by a retrospective cohort study describing the use of CEA (n=15,996) and CAS (n=632) in the HES dataset between 2009-2012.[21] This is likely due to active selection of more co-morbid patients to undergo the less invasive CAS procedure than CEA to minimise risk of complications. This study also supported our finding that older, affluent patients were significantly more likely to receive CEA than CAS.[21] Rates of HTN, IHD and DM were similar to our study in both CEA and CAS cohorts.[21] Lee *et al.*[21] also reported a non-significant increased proportion of White, hypertensive and symptomatic patients undergoing CEA than CAS. This is supported by our

findings which were statistically significant, possibly due to our larger sample size. Other studies have also reported a 3-5-fold higher CEA rate in White versus non-White patients and may be due to cultural barriers to seeking medical attention, mistrust of healthcare professionals, lack of access to healthcare or physician bias.[27-33] However, due to the small sample size of non-White patients in our dataset, further investigation is required to confirm our findings. An analysis of the NIS dataset between 2012-2014 supported our findings that CEA was significantly more common in patients from the highest household income quartile whereas CAS was significantly more common in patients from the lowest household income quartile.[34] This is likely to be due to differences in access to healthcare in more deprived areas. Vogel *et al*.[34] also supported our findings that CEA was significantly more common in older, White patients and those with HTN whereas CAS was significantly more common in those with CHF and cardiac conditions. The large quantity of patients undergoing CEA (n=205,835) and CAS (n=28,990) in that analysis[34] provides substantial power and reliability to their findings that corroborate our results.

Some North American studies have reported different findings to this study. Hussain *et al*.[16] described CAS (n=2,378) being significantly more commonly performed in symptomatic patients compared to CEA (n=14,394) in Ontario between 2002-2014. Patel *et al*.[9] also supported this finding in the CMS dataset between 2003-2006 but reported that IHD and PVD were significantly more common in the CAS cohort (n=7,357) and HTN in CEA patients (n=66,698), consistent with our results. Kim *et al*.[12] described CHF being significantly more common in 1,260,647 CEA patients in the NIS dataset between 2001-2010, in contrast to our findings. However, CEA was significantly more common than CAS (n=124,265) in White patients and those with HTN whilst CAS was significantly more common in those with IHD and PVD[12], consistent with our findings. Dumont and Rughani[14] found that the CAS (n=18,840) patients were more likely to be White than CEA (n=269,321) patients in the NIS

dataset between 1998-2008, in contrast to our results. However, they reported that CEA patients were significantly more likely to be older and suffer from HTN but IHD was significantly more common in CAS patients, similar to our findings. Therefore, minor differences in patients undergoing CEA and CAS in North America compared to England may be due to diverse populations and differing selection criteria for CEA and CAS in each region, different sizes of studies and various datasets being analysed over multiple timeframes. Despite these factors, our findings were also consistent with some North American studies.

Trends in Provision: Temporal

Our finding that the age-standardised CEA rate has reduced by more than 25% since 2011-2012 is supported by a study analysing NVR data in 29,875 patients between 2011-2017.[20] These authors described a 30% decline in the overall CEA rate since 2011, consisting of a 25% reduction in symptomatic patients (86% of cohort) and a 63% decline in asymptomatic patients (14% of the cohort).[20] These results are consistent with our findings in a mainly symptomatic cohort. Our results also support the findings from an earlier study analysing HES data (n=15,996) which showed that the CEA rate steadily increased between 2006-2009.[21]

The CEA rate also appears to be declining in North America, with CEA accounting for the majority of carotid interventions in the USA and Canada (similar to our findings). American Heart Association statistics[19] reported a significant reduction in the annual number of CEAs performed from 154,000 in 1997 to 88,000 in 2013. Between 2001-2010, the carotid revascularisation rate fell from 740 to 490 per million adults (a 34% decrease in the number of CEAs performed).[19] Similar findings have been reported in the literature.[7-13, 16] The reason for this recent temporal decline in CEA rate is unclear. A possible explanation may be improved primary prevention of cerebrovascular disease, with advancement of CMT significantly

reducing risk factors for stroke such as LDL-C, total cholesterol and blood pressure.[35] This resulted in significant decreases in strokes and TIAs caused by large artery atherosclerosis or small vessel disease between 2002-2012.[35] In Scotland, the incidence of cerebrovascular disease has also fallen by 12% in the last decade.[36] Moreover, the prevalence of smoking has been declining. Between 2011-2018, the percentage of English adults smoking cigarettes fell from 19.8% to 14.4%.[37] These factors may have contributed to the 30% reduction in patients presenting with an internal carotid artery stenosis of more than 60% and a 36% reduction in patients presenting with an internal carotid artery stenosis of more than 80% in Ontario between 2002-2014.[38] Another possible reason for the reduction in the age-standardised CEA rate since 2011-2012 in England may be increased centralisation of vascular services, accelerated by Vascular Surgery being recognised as a specialty in its own right in the UK in 2012. Both the VSGBI[39] and GIRFT[40] reports recommended centralisation of vascular services. This may have resulted in a reduction in unnecessary interventions. An increased drive for centralisation and sub-specialty practice, coupled with decreased reimbursement for CEA from 1999-2014 in North America, may have also contributed to a reduced CEA rate.[7, 11] A final possible reason for the reduction in the age-standardised CEA rate since 2011-2012 may be risk aversion leading to more careful patient selection in light of the UK Department of Health's policy of reporting individual Surgeon outcomes annually since 2013.[20] This is supported by a systematic review that suggested Surgeons were more likely to refuse high-risk patients for surgery due to the potential for a procedural complication adversely affecting their published outcomes.[41] Furthermore, due to the uncertainty regarding the role of CEA in asymptomatic patients[42-45], more risk-averse Surgeons may not offer CEA in case of an adverse outcome in a procedure that may not have been necessary. This is particularly relevant in North America where a large proportion of CEAs occur in asymptomatic patients and litigation rates are high.

Our finding that age-standardised CAS rates increased and peaked in 2007-2008 are supported by the findings of another study conducted in the HES dataset between 2006-2009 in 632 patients.[21] Our results are also consistent with a study performed in 231,077 Medicare patients undergoing CAS between 1999-2014 in the CMS dataset.[7] Changes in age-standardised CAS rates over the period of our study may reflect changes in practice informed by RCT findings comparing CEA versus CAS (Figure 6.1 (b)). The initial increase in age-standardised CAS rates until 2007-2008 is likely to have been fuelled by favourable results from early RCTs such as CAVATAS[46] and SAPPHIRE[47] (reported in 2001 and 2004 respectively) which did not report significant differences in procedural outcomes between CEA and CAS. Our results are supported by a Canadian study (n=2,378) that also reported significantly increased CAS rates in Ontario following publication of SAPPHIRE (p=0.01).[16] The fall in age-standardised CAS rates in 2009-2010 is likely due to EVA-3S (published in 2006).[48] This was stopped prematurely due to the RR of any stroke or death within 30 days of treatment being unacceptably high for patients treated with CAS compared to CEA.[48] Results from SPACE-1[49] (also published in 2006) reported no significant difference between CAS and CEA in the composite procedural outcome and may have stabilised age-standardised CAS rates. These increased after CREST-1 was published in 2010 which was the largest of all RCTs and showed no significant difference in the rates of the combined endpoint of stroke, MI or death within 30 days between CAS and CEA.[50] However, age-standardised CAS rates continued to fall once ICSS[51] reported significantly increased incidence of stroke, death or procedural MI in CAS than CEA patients in 2010. This cautious adoption of CAS in England is appropriate given conflicting RCT findings. Until definitive evidence is available suggesting equivalent CEA and CAS procedural outcomes, the age-standardised CAS rate will likely remain low in England. Our finding that the overall proportion of carotid interventions attributable to CAS in England was 3.8% but that this has been increasing since 2009-2010 is supported by other studies.[20, 21]

However, CAS appears to be more commonly performed in North America.[8-16] This difference in uptake of CAS between England and North America may be due to differences in remuneration of hospitals. In the UK, hospitals are paid less for CAS than CEA whereas, in the USA, insurers allow providers to charge more for CAS.[8] Moreover, a conservative culture in the UK may have slowed CAS uptake. However, most studies analysing temporal trends in CAS provision in the USA have not proceeded beyond 2007-2008. Therefore, it is unclear whether CAS provision in the USA would mirror our findings of age-standardised CAS rates decreasing beyond this time, although the proportion of carotid interventions attributable to CAS have been increasing in the UK since 2009-2010 at a smaller rate than the USA.[13, 15]

Trends in Provision: Regional

Our finding that the North West, North East and South West had the highest CEA rate per 100,000 population and London, the South East and East Midlands had the lowest CEA rate per 100,000 population is supported by a study performed in HES data between 2011-2017.[20]

The North West and North East performed CEA and CAS most commonly. This may be due to collaborative working leading to established referral networks between Stroke Physicians, Vascular Surgeons and Interventionalists in high-volume centres. Conversely, the South East had one of the lowest CEA and CAS rates per 100,000 population, suggesting the opposite may be true. Variation in degree of affluence/deprivation may also account for regional disparity in CEA and CAS rates but detailed analysis is beyond the scope of this study, requiring further investigation. Furthermore, the South West and the West Midlands both had one of the lowest CAS rates but one of the highest CEA rates. This suggests a reluctance to embrace CAS as an alternative to CEA in these two regions which requires further investigation.

Similar to our findings, various studies have described regional inequality in the provision of CEA and CAS in the UK[23-25] and internationally.[8, 9, 22] Urban areas have highest CEA and CAS rates whilst rural areas have lowest rates.[8, 9, 24, 25] This may be due to centralisation. However, regional variation in the provision of CEA and CAS should be minimised to provide equality of access, especially as the volume-outcome relationship affects CEA and CAS outcomes.[52, 53]

Regional variation in the provision of thrombolysis has also been demonstrated, accounting for 7-8% of variation in one study.[54, 55] Centralisation was associated with increased odds of receiving thrombolysis within 4.5 hours of symptoms, mainly due to increased use of emergency medical services and more effective referrals.[55] Regional variation in CEA and CAS rates may therefore reduce as centralisation of vascular services progresses throughout England, with potential improvements in the quality of delivery of carotid interventions.

Strengths

The large sample size provides power, validity and reliability to our findings, which are the first temporal and regional analyses of age-standardised CEA and CAS rates in HES data. Age-standardisation (using ONS data) minimised confounding. Stroke admissions have been used as the denominator for CEA rate elsewhere.[20] However, CEA and CAS rates may be affected if the stroke admission rate varies due to changes in guidelines or coding. Cerebrovascular disease is also significantly under-recorded in HES compared to case notes ($p<0.001$).[56]

This study represents an unselected cohort that underwent carotid interventions in England over 16 years with these patients being precisely defined due to standardised coding of diagnoses and procedures. Multiple data sources were also used (including HES and ONS), minimising missing data.

Limitations

The main limitation of this retrospective analysis was the difficulty in defining symptomatic patients due to the inability to differentiate accurately if patients had suffered a new stroke in the territory of their carotid artery ipsilateral to CEA or CAS (laterality is not recorded in HES data). Therefore, our CEA cohort is defined as 99.1% symptomatic which is higher than the national figure of 93.4%.[57] Moreover, HES data only include admitted patients so patients treated for stroke or TIA as outpatients or in the community were not captured. Therefore, the proportion of patients defined as suffering a stroke or TIA prior to CEA in our study is lower than nationally published figures of 38.6% and 45.4% respectively.[57]

There may have also been coding inaccuracies in the early years of the HES dataset. However, a systematic review reported that coding accuracy improved from 77.0% to 86.1% after 2004 with the accuracy of the primary diagnosis significantly increasing ($p=0.02$).[4]

Conclusions and Implications

This 16-year analysis of 68,897 patients undergoing carotid interventions in the HES dataset has shown that there has been a greater than 25% reduction in the age-standardised CEA rate since 2011-2012. There has also been a greater than 20% reduction in the age-standardised CAS rate since 2009-2010. Whilst CEA was more common than CAS overall, older, affluent, White patients were significantly more likely to receive CEA than CAS but patients with CHF, IHD and PVD were significantly more likely to undergo CAS than CEA. Regional variation also existed in the provision of carotid interventions. This is the first age-standardised temporal and regional analysis of CEA and CAS provision in England over 16 years. Further investigation of this study's findings may inform future configuration of vascular services.

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CHAPTER 7: Temporal and Regional Trends in Adjusted Procedural Outcomes following Carotid Interventions in England between 2001-2016 and Assessment of Long-Term Outcomes

Abstract

Background: Trends in procedural and long-term CEA and CAS outcomes are unknown in English patients. This study aimed to: describe temporal and regional trends in CEA and CAS procedural outcomes; identify factors affecting procedural and long-term CEA and CAS outcomes; and assess long-term outcomes.

Methods: Patients receiving CEA or CAS between 2001-2016 were identified in the HES dataset (n=68,897). Multivariate logistic regression was used to adjust procedural outcomes for confounders. Odds ratios and relative risks were calculated for temporal and regional trends respectively. Kaplan-Meier analyses with log-rank tests assessed long-term outcomes. Cox regression identified covariates associated with adverse long-term outcomes.

Results: Between 2001-2016, CEA procedural stroke/death, mortality and LOS significantly improved whilst re-admission worsened. Procedural stroke/death, mortality, stroke and LOS were unchanged over time following CAS but risk of not being discharged home significantly worsened. There was also significant regional variation, mainly for CEA procedural outcomes.

Prior stroke and CHF were associated with significantly worse CEA and CAS procedural outcomes. IHD, PVD, Diabetes Mellitus, Chronic Renal Failure, age 70 years and above and non-White ethnicity were significantly associated with adverse CEA outcomes. Deprivation was associated with significantly increased risk of procedural mortality (p=0.016) and prolonged LOS (p<0.00001) following CEA but did not affect CAS outcomes whilst non-White ethnicity was associated with significantly prolonged LOS following CAS (p<0.00001).

There was overlap between risk factors for procedural and long-term stroke following CEA and CAS. Whilst 20% and 25% of patients had died at 5 years following CEA and CAS respectively, the 5-year stroke rate was less than 10% for both procedures.

Conclusions: This 16-year analysis has identified temporal improvements in most CEA procedural outcomes. Risk factors for adverse procedural and long-term outcomes should be optimised whilst reasons for regional variation in procedural outcomes and differences in long-term post-procedural CEA and CAS outcomes require further investigation.

Introduction

This chapter will focus on factors such as gender, degree of deprivation, ethnicity and comorbidities that may affect CEA and CAS procedural and long-term outcomes. Whilst the previous chapter described temporal and regional trends in CEA and CAS provision, this chapter will describe how CEA and CAS procedural outcomes have changed both temporally and regionally in England between 2001-2016. Long-term CEA and CAS outcomes will also be described.

Background

The effect of gender, deprivation, ethnicity or comorbidities on CEA and CAS procedural outcomes requires clarification due to a paucity of studies that have investigated this association. Patients with severe comorbidities (e.g. CRF) were not recruited into RCTs comparing CEA with CMT or CEA with CAS (in addition to CMT) and there was no meaningful analysis of the effect of patient characteristics (such as degree of deprivation or ethnicity) on procedural outcomes. Females were also under-represented.

There are conflicting findings due to small numbers of patients recruited and the majority of studies being conducted in North America. Findings from these studies are difficult to apply to UK patients as the case-mix undergoing carotid interventions is different (mainly asymptomatic patients undergo carotid revascularisation in the USA compared to mainly symptomatic patients in the UK). Also, CAS is more commonly performed in the USA than the UK which further reduces applicability of findings from North America. There is therefore a need to define associations between gender, degree of deprivation, ethnicity and comorbidities on CEA and CAS outcomes in English patients.

Gender

Older RCTs suggested that female gender is associated with adverse CEA procedural outcomes and that long-term benefit of CEA in preventing strokes is less effective in females compared to males. This is unlikely to be a true effect and may be partly due to stroke incidence and prevalence being 30-40% higher in males compared to females.[1] ACAS initially suggested that females had a non-significantly higher peri-operative stroke/death rate following CEA than males and a lower 5-year event rate for females treated with CMT compared to males.[2] This led to a non-significantly lower 5-year risk reduction for asymptomatic females compared to males.[2] Comparing symptomatic females to males, NASCET demonstrated a higher NNT to prevent one ipsilateral stroke at 5 years (67 versus 12) and one disabling stroke (125 versus 16) due to a significantly higher procedural risk of stroke/death and mortality in females compared to males.[3-5] This was supported by Rothwell *et al*.[6] who reported a 44% increased risk of procedural stroke/death in females undergoing CEA compared to males. Unlike in males, no benefit was found by performing CEA in females with 50-69% symptomatic carotid artery stenosis.[7] Reduced benefit in females receiving CEA compared to males was also supported by ACST-1 which reported males having a lower 5-year stroke risk.[8]

More recent RCTs have shown mixed results. ICSS reported a higher procedural rate of stroke/death/MI for females compared to males at 120 days following CEA but this was lower following CAS.[9] Conversely, CREST-1 reported a non-significant, lower procedural rate of stroke/death, stroke, MI and stroke/death/MI following CEA in females compared to males but this was higher for all CAS outcomes.[10] These findings were repeated in symptomatic patients but asymptomatic males had non-significant superior outcomes compared to asymptomatic females.[10] A subgroup analysis of CREST-1 also reported a non-significant difference in the stroke/death rate following CAS in females compared to males.[11] A pooled CSTC analysis of

3,433 symptomatic patients enrolled in 3 RCTs comparing CEA versus CAS demonstrated higher rates of stroke/death within 120 days of CEA but lower rates of stroke/death within 120 days of CAS in females compared to males.[12]

However, large registry studies have reported no gender differences in CEA or CAS procedural outcomes. Jim *et al.*[13] investigated the effect of gender in 9,865 patients (40.6% female) on CEA (n=6,492) and CAS (n=3,373) outcomes in the Society for Vascular Surgery Vascular Registry. Comparing females to males undergoing CEA, they reported similar rates of procedural mortality, stroke, MI and combined death/stroke/MI.[13] There was also no difference in CEA outcomes when asymptomatic and symptomatic males and females were compared separately (overall OR 1.15 (0.89-1.48); p=0.2958).[13] Procedural stroke/death, mortality, stroke and MI were also similar when comparing CAS outcomes in females versus males.[13] Again, there was no difference in CAS outcomes when asymptomatic and symptomatic males and females were compared separately (overall OR 0.91 (0.68-1.21); p=0.5115).[13] In a German registry study limited to CAS performed between 2012-2014 (n=13,086), female gender was not associated with in-hospital death (RR 1.14 (0.65-1.99); p=0.654), stroke (RR 0.94 (0.72-1.22); p=0.637) or combined stroke/death (RR 0.99 (0.78-1.26); p=0.951).[14] This was supported by a systematic review (n=54,713) that did not report increased risk of stroke/death (RR 0.85 (0.68-1.06); p=0.15) or stroke (RR 1.10 (0.90-1.33); p=0.35) following CAS in females compared to males.[15] However, a large study (n=1,756,445) that used the NIS database between 1998-2012 showed that females were associated with significantly increased procedural risk of in-hospital death and stroke following CAS.[16] Females were also associated with increased risk of procedural stroke following CEA (OR 1.21 (1.11-1.43); p<0.05).[16] However, this study was limited by the use of a small sample (n=5,213) of propensity-scored matched patients who were used to make gender comparisons in CEA and CAS outcomes, resulting in wide CIs, particularly for CAS outcomes.

Smaller, older, single-centre, retrospective studies have shown conflicting results. Whilst the majority have not reported significant differences in CEA procedural outcomes by gender[17-25], others have demonstrated better outcomes in males compared to females.[26-32] However, this gender effect was confounded by symptom status in one study[27], may have been influenced by ethnicity elsewhere[30] and was of questionable clinical significance in other studies.[28, 31] A meta-analysis has shown that case series with gender as a secondary outcome were significantly more likely to report increased procedural stroke/death rates following CEA in females compared to males (OR 1.39 (1.15-1.68); p=0.001).[33] However, if gender was the primary aim, no significant differences were reported in CEA outcomes between females and males in either case series (OR 1.20 (0.93-1.56; p=0.168) or databases (OR 1.03 (0.96-1.10); p=0.474).[33] This highlights the need to interpret underpowered subgroup analyses with caution.

Therefore, there is uncertainty regarding the effect of gender on CEA and CAS procedural outcomes, necessitating a systematic review of RCTs to clarify the association in symptomatic patients.[34] It appears that adverse CEA outcomes in females may be due to underpowered subgroup analyses of RCT findings, causing potential statistical artefact. This may explain why large registry studies, representing routine practice and large statistical power, have reported no difference in CEA or CAS procedural outcomes in females compared to males. RCTs also report data collected in the 1980s. Analyses from large administrative datasets (e.g. HES) may be more generalisable to current practice, providing clarity regarding the association between gender and CEA and CAS procedural outcomes.

Deprivation

Vogel *et al*.[35] analysed the effect of deprivation on CEA (n=205,835) and CAS (n=28,990) outcomes, using the NIS dataset between 2012-2014. Lowest income quartile patients were significantly more likely to receive CAS compared to high income patients (OR 1.32 (1.27-1.37)).[35] Lee *et al*.[36] also reported higher deprivation being significantly associated with CAS use ($p<0.001$). Overall in-hospital mortality following carotid intervention was significantly higher in the lowest income quartile compared to the highest, irrespective of ethnicity (0.3% versus 0.2% respectively; OR 1.64 (1.25-2.14); $p=0.0004$).[35] The lowest income quartile was also significantly more likely to suffer a procedural stroke following CEA and CAS than the highest quartile (OR 1.16 (1.06-1.28); $p=0.0018$) and LOS in the lowest income quartile was significantly prolonged ($p<0.0001$).[35] In an older study, MacKenzie *et al*.[37] compared rates of admission of 1,203 symptomatic patients with the CEA rate in patients from varying household income backgrounds in Scotland between 1995-2000. Patients from more deprived backgrounds were significantly more likely to present with neurological symptoms ($p<0.001$) whilst the admission rate was significantly less than the most affluent group ($p<0.005$).[37] However, this was not reflected in the CEA rate, which was higher in the most affluent groups.[37]

These findings suggest that there may be differences in CEA and CAS outcomes, possibly partly contributed by variations in the provision of carotid interventions with degree of affluence/deprivation. However, these studies are limited by being performed in the USA[35] (not representing English practice) or not examining the effect of the degree of deprivation on outcomes following carotid intervention.[36, 37]

Ethnicity

Various studies have reported increased rates of procedural stroke and death in non-White compared to White patients undergoing CEA and CAS.[35, 38-46] This has been partly attributed to increased rates of DM, HTN, CRF, previous stroke, angina and CHF in non-White compared to White patients.[40, 42-47] However, some studies have reported that complications following CAS may be comparable between White and non-White patients.[47, 48] This may be due to the less invasive CAS protecting against the effect of comorbidities on outcomes but the majority of studies are based in North America where the case-mix is different to the UK. Findings are further limited by most studies being conducted more than 10 years ago.

An English study undertaken in the last decade reported worse outcomes in non-White English adults undergoing carotid intervention compared to White counterparts.[36] In a sample of patients undergoing CEA (n=15,996) and CAS (n=632) between 2009-2012, non-White patients were significantly more likely to have prolonged LOS (p=0.003).[36] However, no further details (e.g. comorbidities) were provided for ethnic groups compared to White patients and there was no comparison of procedural stroke or mortality rates.

Comorbidities

Conflicting results have been reported regarding the effect of comorbidities on CEA and CAS procedural outcomes. Whilst DM has been shown to predict significantly worse CEA and CAS outcomes in some studies[12, 49-55], others reported similar outcomes between diabetic and non-diabetic patients undergoing carotid intervention.[6, 56-59] PVD may also predict significantly worse CEA and CAS outcomes[6, 15, 50, 51] though not consistently.[12] This is unlike HTN, which has consistently been associated with adverse CEA and CAS outcomes.[6, 12, 15, 50]

IHD was also reported to increase CEA and CAS procedural risk[15, 51, 60] but this was not always statistically significant.[6, 12, 50, 61] Subclinical coronary artery disease was not associated with significantly increased risk of procedural death (1.2% versus 0.5%; p=0.38), stroke (0.0% versus 1.4%; p=0.61) or MI (1.2% versus 0.0%; p=0.11) following CEA.[62] Whilst subclinical coronary artery disease significantly increased risk of cardiac damage following CEA (13.6% versus 0.5%; p<0.01), there was no effect on long-term survival (p=0.752).[62]

CRF has been associated with significantly worse CEA and CAS outcomes.[49, 63-69] This was most pronounced in patients with severe CRF (including end-stage renal disease).[70-72] However, Protack *et al*.[73] reported no significant difference in rates of mortality (p=0.37), stroke (p=0.55) or MI (p=0.41) in patients with and without CRF undergoing CEA. In patients undergoing CAS, mortality (15.4% versus 3.3% versus 1.0%; p=0.02) and stroke rate (23.1% versus 3.3% versus 4.1%; p=0.01) was significantly higher in patients with severe CRF compared to moderate CRF and healthy controls respectively.[73]

Rationale for Study

Due to the conflicting results described above, clarity is required about the effect of gender, degree of deprivation, ethnicity and comorbidities on CEA and CAS procedural outcomes in English patients. If factors can be identified that are associated with adverse outcomes following carotid intervention, these could be optimised.

Studies have also demonstrated temporal improvements in CEA and CAS outcomes.[38, 48, 74-78] However, a systematic review reported that procedural mortality following CEA in symptomatic patients had worsened in the last decade. The overall risk of procedural mortality was 1.4% (1.2-1.6)[79], which is greater than reported in the pooled analysis of data from ECST[80]

and NASCET[81] (1.0% (0.9-1.1)). This might be explained by a significant increase in the age of symptomatic patients undergoing CEA (from 60.9 to 70.3 years old; p<0.00001).[79]

Moreover, to date, no study has described long-term CEA and CAS outcomes in English patients. RCTs reported significantly lower stroke/death rates following CEA than CAS in studies that ranged from 4-10 years follow-up.[82-85] A meta-analysis of 7,005 patients[86] showed that this is likely due to significantly increased procedural risk of non-disabling stroke following CAS than CEA, supported by CREST-1's finding that more than half of all ipsilateral strokes that occurred following CAS over a 10-year period were within the first 30 days.[85] In studies that did not detect a significant difference in procedural stroke rates between CEA and CAS or excluded the peri-procedural period, long-term ipsilateral stroke rates were similar[82, 84, 85, 87-90], suggesting that both interventions have comparable durability. This was confirmed by a meta-analysis of CAVATAS, EVA-3S and SPACE-1 that reported a non-significant difference in long-term risk of non-peri-operative ipsilateral stroke comparing CAS with CEA (OR 1.18 (0.70-1.99); p=0.54).[88] A recent pooled analysis from EVA-3S, SPACE-1, ICSS and CREST-1 that followed 4,754 patients up to 12.4 years, also reported significantly higher procedural rates of ipsilateral stroke/death, minor stroke and all stroke following CAS versus CEA but similar post-procedural rates for all outcomes.[91] An analysis of a Canadian administrative dataset also reported significantly higher stroke/death, mortality and stroke rates following CAS at 13 years follow-up in 15,525 patients, driven by significantly higher procedural stroke and death risk following CAS compared to CEA.[92] However, these adverse outcomes were sustained even when the peri-procedural period was excluded, leading to a significantly higher long-term post-procedural risk of any stroke/death, mortality and stroke following CAS versus CEA respectively.[92] A significantly higher risk of post-procedural stroke/death, ipsilateral stroke/death and ipsilateral stroke following CAS versus CEA was also reported by a Swedish Vascular Registry study that analysed 1,157 patients for a median of 4.1

years.[93] An American study in 9,309 Medicare patients reported a significantly higher unadjusted 3-year mortality and stroke/TIA rate following CAS than CEA but outcomes were comparable when adjusted for patient- and provider-level characteristics[94] whilst a single-centre study reported no differences in 7-year survival or stroke following CEA and CAS.[95]

Therefore, clarity is required regarding temporal and regional trends in procedural outcomes following CEA and CAS in English patients and assessment of long-term outcomes. Such a study has never been performed.

Aim

This study aimed to use HES data (linked to ONS mortality records) to: describe temporal and regional trends in procedural CEA and CAS outcomes in England between 2001-2016; clarify the effect of gender, degree of deprivation, ethnicity and comorbidities on CEA and CAS procedural and long-term outcomes; and assess long-term CEA and CAS outcomes.

Methods

Definition of the study population, baseline characteristics, comorbidities and stratification of the dataset into 2-year groups and regions have been described in Chapter 6.

Logistic Regression Analyses

Univariate logistic regression identified significant associations between all CEA and CAS procedural outcomes and age, gender, IMD score (marker of degree of affluence/deprivation), ethnicity, comorbidities and symptom status. Age was divided into less than 60 years (baseline), 60-69 years and 70 years and above. IMD score was divided into quintiles (quintile 1 was used as the baseline as it represented the most affluent group) and White patients (baseline) were compared with non-White patients. Having CHF, IHD, PVD, HTN, DM or CRF preceding CEA or CAS was also compared with controls for each outcome. The effect of a previous stroke, TIA or other symptoms (both individually and collectively) was also compared with controls for each outcome.

This allowed the identification of factors that may cause heterogeneity in outcomes, allowing a specific multivariate model to be produced for each outcome, according to procedure type. Thereafter, logistic regression was performed to produce adjusted ORs comparing all 2-year groups with the first (2001-2002), providing temporal trends for each procedural outcome.

For regional trends in outcomes, ORs were transformed into RRs, using 'floating absolute risk' methodology, to allow independent comparisons between all regions. This is an established methodology in epidemiological research.[96] The North East region was used as the baseline for this analysis (RR 1.00). Inverse variance weighing was used to calculate an 'average' RR for all regions, acting as a reference point that each region could be compared against.

Study Outcomes

Primary procedural outcomes were temporal and regional trends in the odds of 30-day mortality and stroke (considered separately and combined) following CEA or CAS. Secondary procedural outcomes were temporal and regional trends in the odds of LOS greater than 2 days, re-admission within 30 days of the procedure and being discharged other than home (a marker of procedural complications). All procedural outcomes were adjusted for confounding factors.

Long-term outcomes were 5-year mortality and stroke rates (considered separately).

Statistics

ORs with 95% CIs are provided for each logistic regression analysis for each 2-year group per procedural outcome. RRs with 95% CIs are presented for each floating absolute risk analysis for each region per procedural outcome. The 2-year group 2001-2002 (OR 1.00) and the North-East (RR 1.00) were reference groups in all temporal and regional analyses respectively.

Time-to-event data were used to perform Kaplan-Meier analyses (with 95% CIs) to estimate the event-free probability over 5 years for long-term CEA and CAS outcomes, including and excluding the peri-procedural period. Log-rank tests compared differences between treatment groups at 30 days post-procedure (where applicable) and annually for each outcome. Cox's proportional hazards regression model was used to identify covariates that were associated with adverse long-term outcomes (expressed as HRs).

A p-value ≤ 0.05 was deemed statistically significant. All analyses were performed using Stata, version 15.1 (StataCorp LLC, Texas, USA).

Results

Overall, crude outcomes were superior following CEA than CAS (Table 7.1). Procedural stroke/death, mortality and stroke were all lower in CEA than CAS patients (Table 7.1). LOS was comparable but 30-day re-admission was lower following CEA than CAS (Table 7.1). A higher proportion of patients were discharged home following CEA whereas a higher proportion of patients were discharged to a ward/care home following CAS (Table 7.1).

Table 7.1: Crude outcomes in patients undergoing CEA and CAS in the HES dataset between 2001-2016.

Outcomes	CEA (n=66,267)	CAS (n=2,630)
Primary Outcomes		
30-day combined stroke/death (n, %)	1,474 (2.2)	144 (5.5)
30-day mortality (n, %)	640 (1.0)	87 (3.3)
30-day stroke (n, %)	864 (1.3)	62 (2.4)
Secondary Outcomes		
Median LOS (IQR)	2 (1-4)	2 (1-4)
30-day re-admission (n, %)	7,551 (11.4)	454 (17.3)
Discharged home (n, %)	62,922 (95.0)	2,254 (85.7)
Discharged LA residential accommodation (n, %)	62 (0.1)	0 (0.0)
Discharged NHS ward/care home (n, %)	1,871 (2.8)	223 (8.5)
Discharged non-NHS care home/hospital (n, %)	231 (0.3)	16 (0.6)
Discharged non-NHS hospice (n, %)	5 (0.0)	1 (0.0)

Abbreviations – CAS: Carotid Artery Stenting; CEA: Carotid Endarterectomy; IQR: Inter-Quartile Range; LOS: Length of Stay; NHS: National Health Service.

Table 7.2 lists the main causes of re-admission following CEA and CAS.

Table 7.2: Most frequent causes of 30-day re-admission following carotid intervention.

Reason for re-admission	n	Rate (%)
Cerebral infarction/stroke/hemiplegia	892	1.3
Angina/CAD/Chest pain/MI	583	0.8
Haematoma/neck swelling	473	0.7
Urinary retention/UTI/catheter change/Haematuria/BPH	335	0.5
TIA	246	0.4
Dyspnoea/pneumonia/LRTI/IECOPD	237	0.3
Syncope/hypotension/dizziness	235	0.3
Infection/Dehiscence/Paraesthesia	216	0.3
Headache	169	0.2
Intracerebral haemorrhage/SAH	101	0.1

Abbreviations – BPH: Benign Prostatic Hyperplasia; CAD: Coronary Artery Disease; IECOPD: Infective Exacerbation of Chronic Obstructive Pulmonary Disease; LRTI: Lower respiratory Tract Infection; MI: Myocardial Infarction; SAH: Subarachnoid Haemorrhage; TIA: Transient Ischaemic Attack; UTI: Urinary Tract Infection.

Predictors of Adverse CEA Procedural Outcomes

Results from multivariate regression analyses identified factors associated with adverse CEA procedural outcomes. Some factors were associated with reduced risk of stroke/death, prolonged LOS and re-admission following CEA (Tables 7.3 (a), 7.4 and 7.5).

Prior stroke and age 70 years and above were associated with procedural complications for each outcome. CHF, IHD, PVD, DM, CRF and non-White ethnicity were also associated with adverse CEA outcomes. Increased deprivation appeared to be associated with increased risk of procedural mortality and prolonged LOS (Tables 7.3 (b) and 7.4). Female gender appeared to be associated with increased risk of stroke, prolonged LOS, re-admission and not being discharged home following CEA (Tables 7.3 (c), 7.4, 7.5 and 7.6).

Table 7.3 (a): Factors associated with 30-day stroke/death following CEA. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,329 (59.4)	1,013	1.79	1.45-2.21	**p<0.0001**
Age 60-69 years	18,877 (28.5)	345	1.33	1.06-1.67	**p=0.013**
Female	21,653 (32.7)	503	1.07	0.96-1.19	p=0.231
Non-White	2,497 (4.0)	78	1.38	1.09-1.75	**p=0.007**
Prior Stroke	17,770 (26.8)	683	3.38	2.57-4.45	**p<0.0001**
Prior TIA	13,856 (20.9)	269	1.47	1.15-1.89	**p=0.002**
Prior Stroke/TIA	31,626 (47.7)	952	0.65	0.48-0.88	**p=0.005**
CHF	2,865 (4.3)	156	2.12	1.76-2.55	**p<0.00001**
IHD	20,312 (30.7)	569	1.15	1.02-1.29	**p=0.024**
PVD	7,253 (10.9)	224	1.32	1.13-1.54	**p<0.0001**
HTN	44,997 (67.9)	1,105	1.15	1.01-1.30	**p=0.038**
DM	14,137 (21.3)	407	1.17	1.04-1.33	**p=0.012**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; DM: Diabetes Mellitus; HTN: Hypertension; IHD: Ischaemic Heart Disease; OR: Odds Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Table 7.3 (b): Factors associated with 30-day mortality following CEA. Baseline comparison for age was less than 60 years and baseline comparison for degree of deprivation was IMD1. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,329 (59.4)	464	2.79	1.88-4.14	**p<0.0001**
Age 60-69 years	18,877 (28.5)	139	1.81	1.19-2.75	**p=0.006**
Female	21,653 (32.7)	190	0.87	0.73-1.03	p=0.105
IMD4	13,187 (20.0)	145	1.39	1.06-1.81	**p=0.016**
Non-White	2,497 (4.0)	37	1.56	1.11-2.20	**p=0.010**
Prior Stroke	17,770 (26.8)	245	1.81	1.40-2.36	**p<0.00001**
Prior Stroke/TIA	31,626 (47.7)	359	0.84	0.65-1.08	p=0.167
CHF	2,865 (4.3)	111	3.25	2.57-4.12	**p<0.00001**
IHD	20,312 (30.7)	313	1.56	1.31-1.87	**p<0.00001**
PVD	7,253 (10.9)	120	1.50	1.21-1.87	**p<0.0001**
CRF	3,305 (5.0)	70	1.37	1.04-1.81	**p=0.024**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; IHD: Ischaemic Heart Disease; IMD: Index of Multiple Deprivation; OR: Odds Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Table 7.3 (c): Factors associated with 30-day stroke following CEA. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,329 (59.4)	571	1.43	1.12-1.83	**p=0.004**
Age 60-69 years	18,877 (28.5)	212	1.17	0.90-1.53	p=0.244
Female	21,653 (32.7)	321	1.20	1.04-1.38	**p=0.013**
Prior Stroke	17,770 (26.8)	447	2.64	2.14-3.25	**p<0.0001**
Prior Stroke/TIA	31,626 (47.7)	613	1.11	0.90-1.39	p=0.331
HTN	44,997 (67.9)	647	1.19	1.01-1.10	**p=0.038**
DM	14,137 (21.3)	242	1.27	1.08-1.48	**p=0.003**

Abbreviations – CI: Confidence Interval; DM: Diabetes Mellitus; HTN: Hypertension; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.4: Factors associated with LOS greater than 2 days following CEA. Baseline comparison for age was less than 60 years and baseline comparison for degree of deprivation was IMD1. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,308 (59.4)	17,392	1.60	1.52-1.69	**p<0.00001**
Age 60-69 years	18,870 (28.5)	6,889	1.18	1.11-1.25	**p<0.00001**
Female	21,640 (32.7)	9,757	1.34	1.30-1.39	**p<0.00001**
IMD5	13,183 (20.0)	5,806	1.28	1.21-1.34	**p<0.00001**
IMD4	13,178 (20.0)	5,581	1.18	1.12-1.24	**p<0.00001**
IMD3	13,189 (20.0)	5,307	1.10	1.05-1.16	**p<0.00001**
Non-White	2,494 (4.0)	1,276	1.49	1.37-1.62	**p<0.00001**
Prior Stroke	17,762 (26.8)	8,833	1.53	1.46-1.61	**p<0.0001**
Prior Stroke/TIA	31,626 (47.7)	14,530	0.78	0.66-0.92	**p=0.004**
Ever symptomatic	34,001 (51.3)	12,159	0.69	0.58-0.81	**p<0.00001**
CHF	2,864 (4.3)	1,657	1.64	1.51-1.78	**p<0.00001**
IHD	20,301 (30.7)	9,441	1.30	1.26-1.35	**p<0.00001**
PVD	7,251 (10.9)	3,349	1.19	1.13-1.26	**p<0.00001**
HTN	44,977 (67.9)	18,645	0.94	0.91-0.98	**p=0.0009**
DM	14,129 (21.3)	6,266	1.07	1.03-1.12	**p=0.0014**
CRF	3,304 (5.0)	1,618	1.09	1.01-1.18	**p=0.021**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; HTN: Hypertension; IHD: Ischaemic Heart Disease; IMD: Index of Multiple Deprivation; LOS: Length of Stay; OR: Odds Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Table 7.5: Factors associated with 30-day re-admission following CEA. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,329 (59.4)	4,870	1.15	1.06-1.24	**p=0.001**
Age 60-69 years	18,877 (28.5)	1,871	0.96	0.88-1.05	p=0.393
Female	21,653 (32.7)	2,535	1.07	1.01-1.12	**p=0.0156**
Non-White	2,497 (4.0)	362	1.20	1.07-1.35	**p=0.002**
Prior Stroke	17,770 (26.8)	2,717	1.47	1.37-1.58	**p<0.0001**
Prior Stroke/TIA	31,626 (47.7)	4,326	0.83	0.65-1.06	p=0.142
Ever symptomatic	34,018 (51.3)	3,142	0.75	0.59-0.95	**p=0.018**
CHF	2,865 (4.3)	547	1.39	1.25-1.54	**p<0.00001**
IHD	20,312 (30.7)	2,907	1.32	1.25-1.39	**p<0.00001**
PVD	7,253 (10.9)	1,034	1.18	1.09-1.27	**p<0.00001**
HTN	44,997 (67.9)	5,516	1.11	1.05-1.17	**p<0.00001**
DM	14,137 (21.3)	1,993	1.19	1.13-1.27	**p<0.00001**
CRF	3,305 (5.0)	619	1.41	1.28-1.56	**p<0.00001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; HTN: Hypertension; IHD: Ischaemic Heart Disease; OR: Odds Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Table 7.6: Factors associated with not being discharged home following CEA. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	39,329 (59.4)	2,352	1.58	1.39-1.80	**p<0.00001**
Age 60-69 years	18,877 (28.5)	682	1.01	0.87-1.17	p=0.908
Female	21,653 (32.7)	1,172	1.14	1.06-1.24	**p=0.0006**
Non-White	2,497 (4.0)	186	1.37	1.16-1.61	**p<0.0001**
Prior Stroke	17,770 (26.8)	2,014	4.42	3.92-4.99	**p<0.0001**
Prior Stroke/TIA	31,626 (47.7)	2,557	1.05	0.92-1.19	p=0.486
CHF	2,865 (4.3)	321	1.93	1.69-2.22	**p<0.00001**
IHD	20,312 (30.7)	1,249	1.21	1.11-1.31	**p<0.00001**
PVD	7,253 (10.9)	437	1.16	1.04-1.30	**p=0.010**
DM	14,137 (21.3)	920	1.17	1.08-1.28	**p<0.00001**
CRF	3,305 (5.0)	292	1.26	1.10-1.45	**p=0.001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; IHD: Ischaemic Heart Disease; OR: Odds Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Predictors of Adverse CAS Procedural Outcomes

Results from multivariate regression analyses identified factors associated with adverse CAS procedural outcomes. Some factors were associated with reduced risk of procedural stroke/death, mortality, prolonged LOS and not being discharged home following CAS (Tables 7.7 (a), 7.7 (b), 7.8 and 7.10).

Prior stroke was associated with procedural complications for each outcome. CHF was also associated with adverse CAS outcomes. Age 70 years and above was associated with increased risk of procedural stroke (Table 7.7 (c)). Increased deprivation was not associated with any adverse outcomes whilst non-White ethnicity and female gender were both associated with increased risk of prolonged LOS following CAS (Table 7.8).

Table 7.7 (a): Factors associated with 30-day stroke/death following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,224 (46.7)	75	0.98	0.64-1.51	p=0.927
Age 60-69 years	822 (31.4)	30	0.55	0.33-0.93	**p=0.025**
Female	904 (34.4)	59	1.35	0.96-1.90	p=0.087
Prior Stroke	750 (28.5)	81	3.41	1.92-6.04	**p<0.0001**
Prior Stroke/TIA	1,303 (49.5)	112	1.02	0.56-1.85	p=0.956
CHF	196 (7.5)	23	2.77	1.69-4.53	**p<0.0001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.7 (b): Factors associated with 30-day mortality following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,224 (46.7)	39	0.59	0.35-1.00	p=0.051
Age 60-69 years	822 (31.4)	17	0.36	0.19-0.70	**p=0.002**
Female	904 (34.4)	36	1.36	0.88-2.10	p=0.163
Prior Stroke	750 (28.5)	55	3.24	1.62-6.50	**p=0.001**
Prior Stroke/TIA	1,303 (49.5)	78	1.50	0.70-3.25	p=0.300
CHF	196 (7.5)	16	3.80	2.09-6.90	**p<0.0001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.7 (c): Factors associated with 30-day stroke following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,224 (46.7)	38	2.34	1.08-5.05	**p=0.031**
Age 60-69 years	822 (31.4)	15	1.24	0.51-2.98	p=0.633
Female	904 (34.4)	24	1.21	0.72-2.03	p=0.467
Prior Stroke	750 (28.5)	28	3.49	1.33-9.15	**p=0.011**
Prior Stroke/TIA	1,303 (49.5)	37	0.55	0.21-1.44	p=0.224

Abbreviations – CI: Confidence Interval; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.8: Factors associated with LOS greater than 2 days following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,223 (46.7)	404	0.58	0.46-0.73	**p<0.00001**
Age 60-69 years	822 (31.4)	262	0.56	0.44-0.72	**p<0.00001**
Female	903 (34.3)	400	1.66	1.38-1.99	**p<0.00001**
Non-White	135 (5.4)	84	2.72	1.84-4.02	**p<0.00001**
Prior Stroke	750 (28.5)	429	2.15	1.67-2.76	**p<0.0001**
Prior Stroke/TIA	1,303 (49.6)	675	0.71	0.46-1.10	p=0.124
Ever symptomatic	1,216 (46.3)	233	0.33	0.22-0.50	**p<0.0001**
CHF	196 (7.5)	96	2.09	1.51-2.89	**p<0.00001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; LOS: Length of Stay; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.9: Factors associated with 30-day re-admission following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,224 (46.7)	221	1.12	0.85-1.48	p=0.416
Age 60-69 years	822 (31.4)	130	0.96	0.71-1.30	p=0.808
Female	904 (34.4)	169	1.23	0.99-1.53	p=0.063
Prior Stroke	750 (28.5)	162	1.39	1.02-1.89	**p=0.039**
Prior Stroke/TIA	1,303 (49.5)	263	1.12	0.84-1.50	p=0.443
CHF	196 (7.5)	52	1.66	1.17-2.35	**p=0.005**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

Table 7.10: Factors associated with not being discharged home following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	OR	95% CIs	p-value
Age ≥70 years	1,224 (46.7)	148	0.57	0.43-0.77	**p<0.0001**
Age 60-69 years	822 (31.4)	96	0.57	0.41-0.79	**p=0.001**
Female	904 (34.3)	151	1.28	1.00-1.65	p=0.055
Prior Stroke	750 (28.5)	225	4.85	2.88-8.17	**p<0.0001**
Prior TIA	553 (21.0)	102	1.58	0.98-2.53	p=0.058
Prior Stroke/TIA	1,303 (49.5)	327	0.81	0.35-1.87	p=0.626

Abbreviations – CI: Confidence Interval; OR: Odds Ratio; TIA: Transient Ischaemic Attack.

CEA Procedural Outcomes: Temporal Trends

The odds of combined procedural stroke/death following CEA (Figure 7.1 (a)) have reduced over time, reaching statistical significance in 2011-2012 ($p=0.05$). This may be due to the odds of procedural mortality (Figure 7.1 (b)) reducing over time, being statistically significant since 2011-2012 (all $p<0.0001$). However, procedural stroke risk (Figure 7.1 (c)) has increased, reaching statistical significance in 2013-2014 ($p=0.043$). LOS greater than 2 days (Figure 7.2) has significantly improved over time ($p<0.0001$ for all year groups) but re-admission following CEA (Figure 7.3) has worsened since 2001-2002, reaching statistical significance in 2007-2008 ($p=0.014$) and peaking in 2011-2012 ($p<0.0001$). It improved slightly subsequently but remained significantly worse in 2013-2014 ($p=0.003$) and 2015-2016 ($p=0.022$) compared to 2001-2002. The odds of being discharged home following CEA (Figure 7.4) have not changed overall but were significantly improved in 2015-2016 ($p=0.041$).

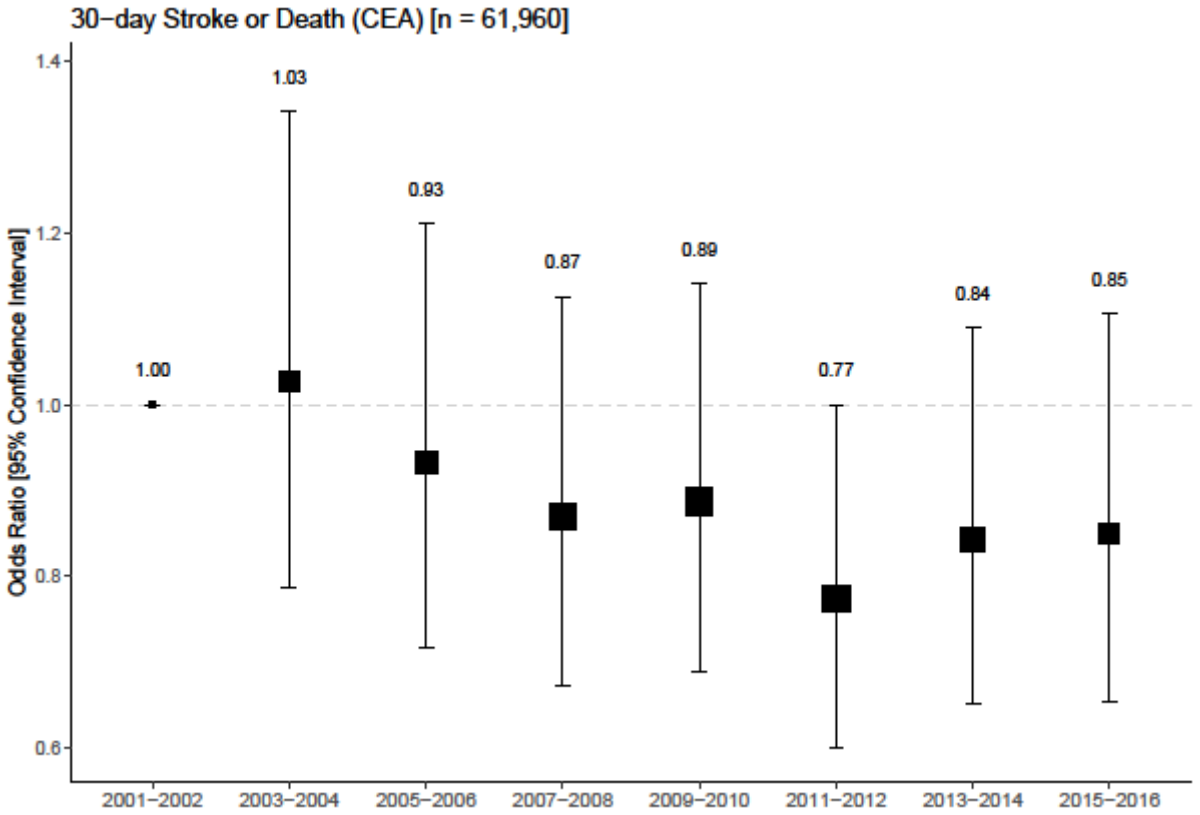

Figure 7.1 (a): Temporal trend in the OR (with 95% CIs) of 30-day stroke/death following CEA in the HES dataset between 2001-2016.

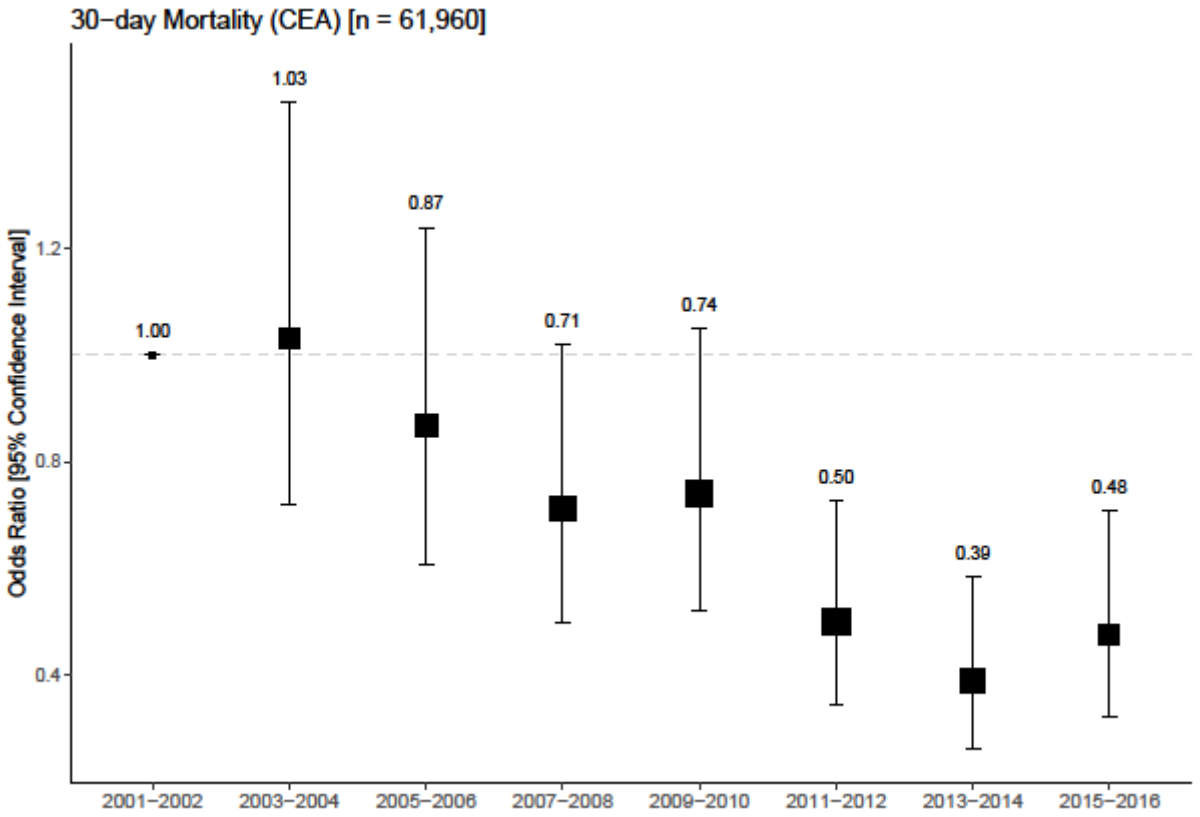

Figure 7.1 (b): Temporal trend in the OR (with 95% CIs) of 30-day mortality following CEA in the HES dataset between 2001-2016.

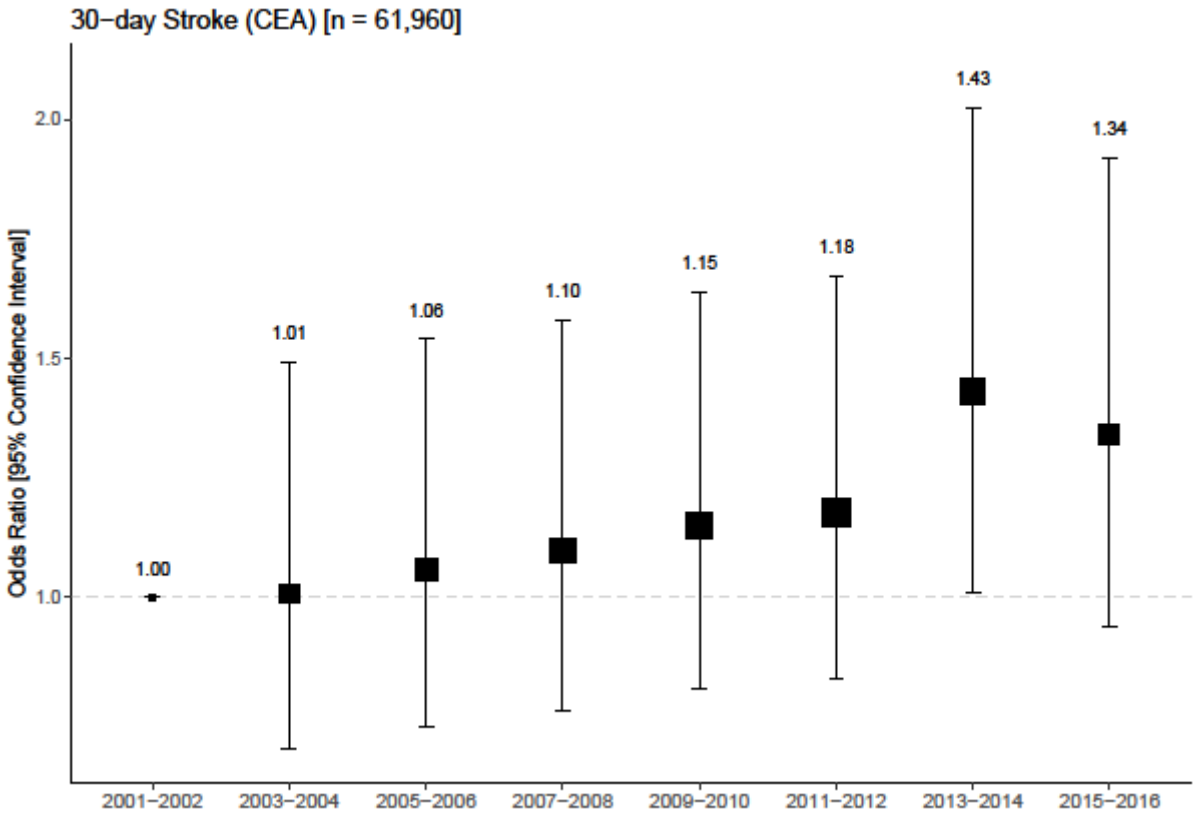

Figure 7.1 (c): Temporal trend in the OR (with 95% CIs) of 30-day stroke following CEA in the HES dataset between 2001-2016.

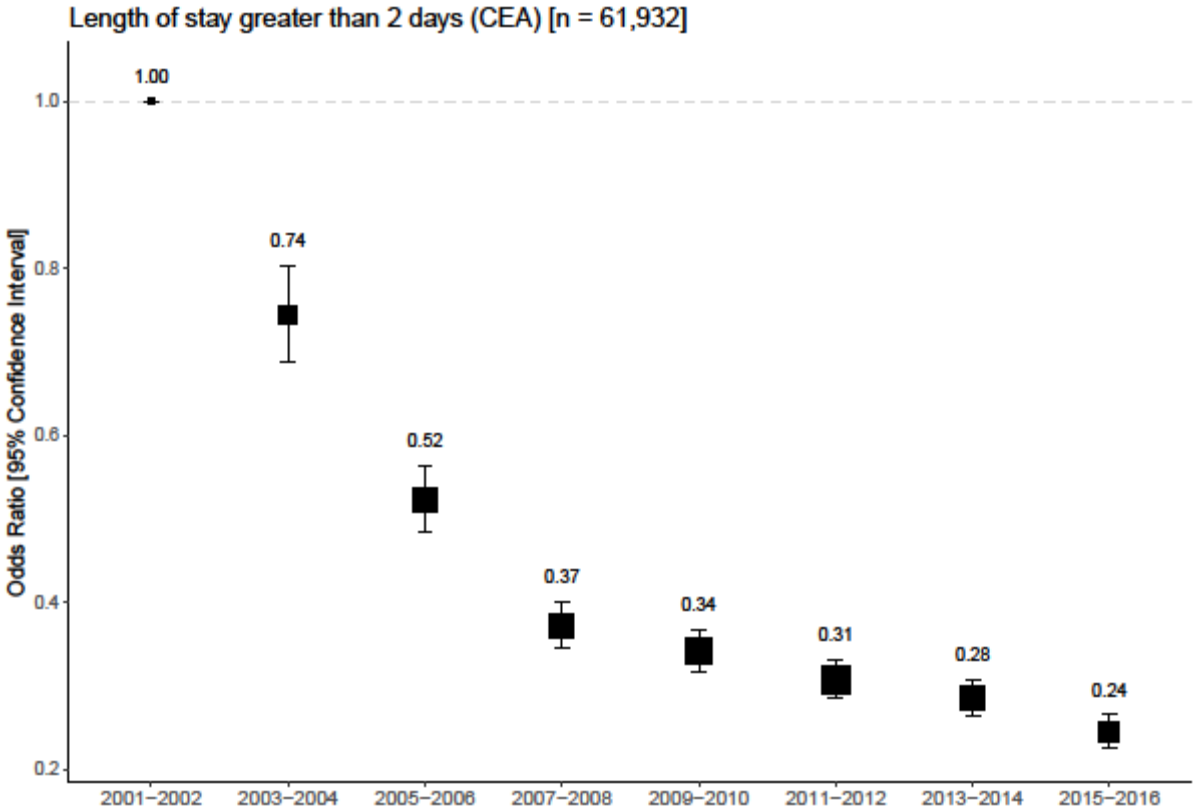

Figure 7.2: Temporal trend in the OR (with 95% CIs) of LOS greater than 2 days following CEA in the HES dataset between 2001-2016.

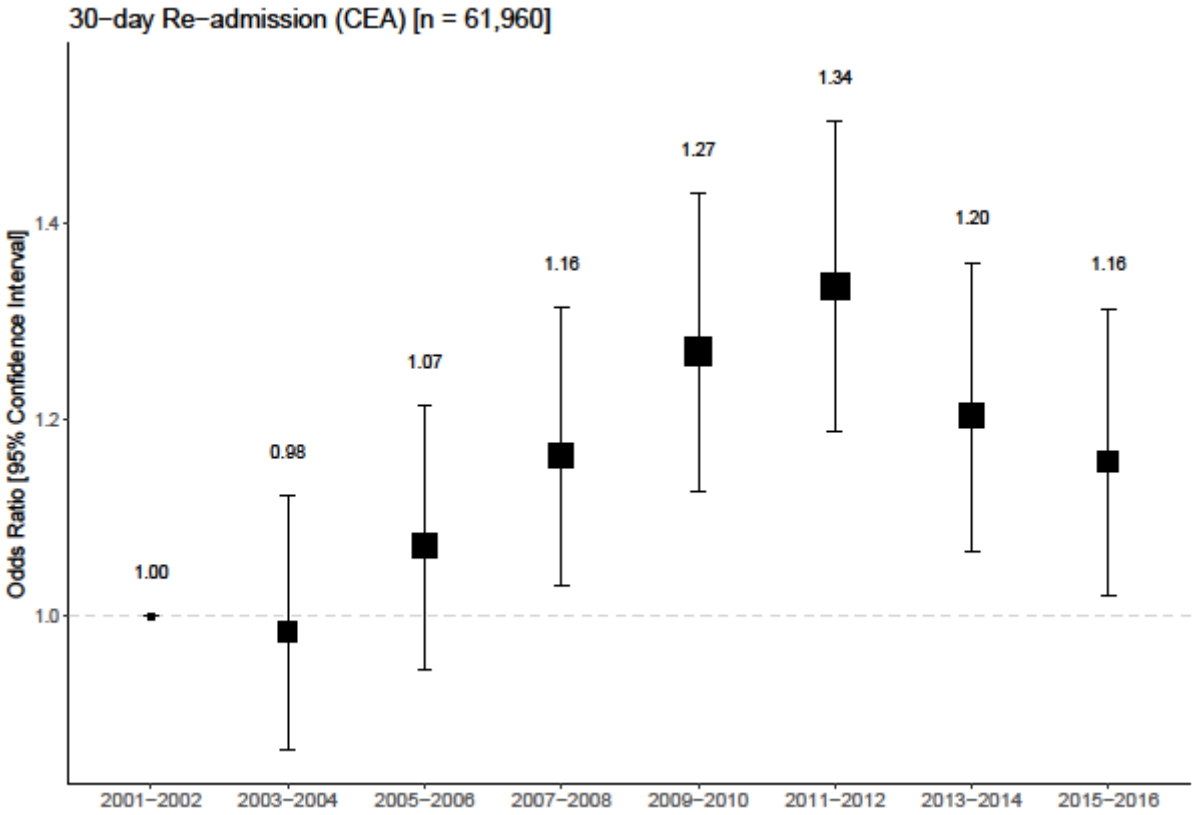

Figure 7.3: Temporal trend in the OR (with 95% CIs) of 30-day re-admission following CEA in the HES dataset between 2001-2016.

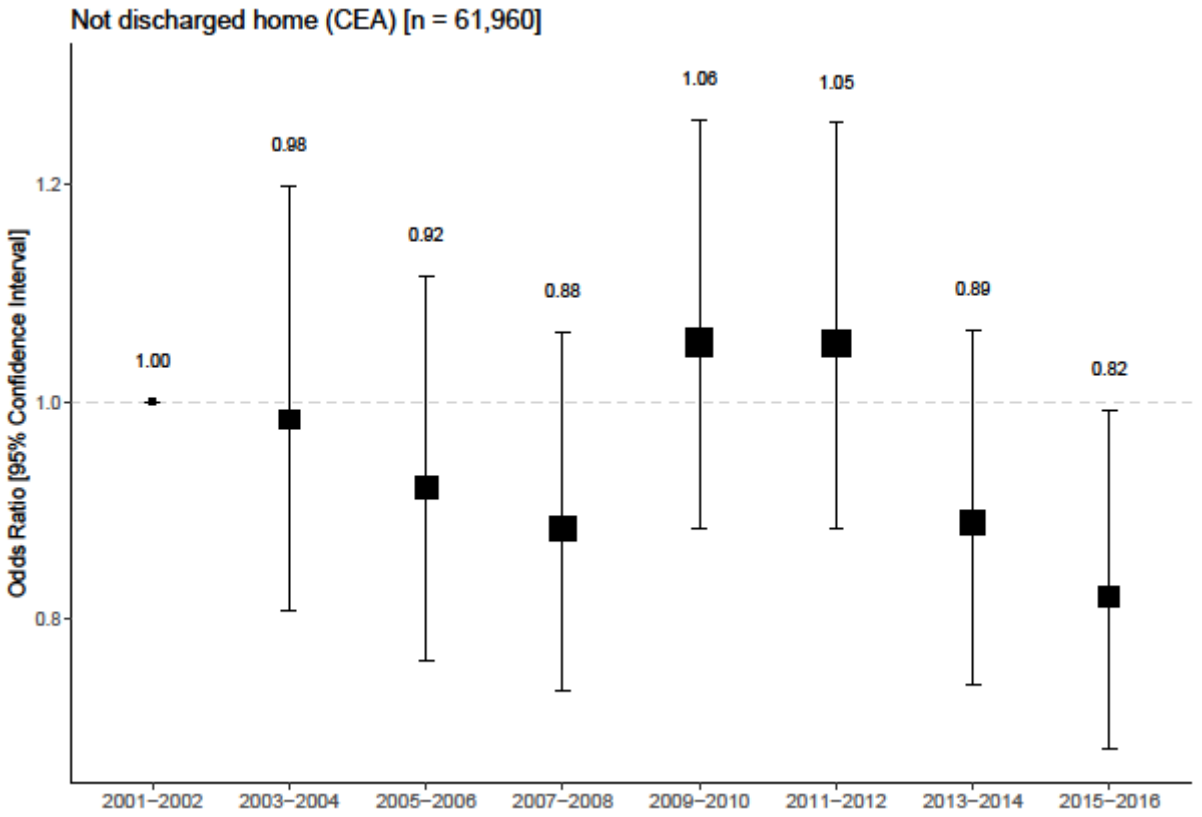

Figure 7.4: Temporal trend in the OR (with 95% CIs) of not being discharged home following CEA in the HES dataset between 2001-2016.

CAS Procedural Outcomes: Temporal Trends

The odds of combined procedural stroke/death, mortality, stroke and prolonged LOS following CAS (Figures 7.5 (a), 7.5 (b), 7.5 (c) and 7.6) have not significantly changed over time. Re-admission following CAS (Figure 7.7) has tended to worsen, reaching statistical significance in 2011-2012 (p=0.024), before improving slightly. The odds of not being discharged home (Figure 7.8) have significantly worsened each year since 2003-2004. This reached statistical significance in 2005-2006 (p=0.009) and remained significant throughout all study years (p=0.004 in 2007-2008 and p=0.001 since 2009-2010). These results should be interpreted with caution due to their wide CIs.

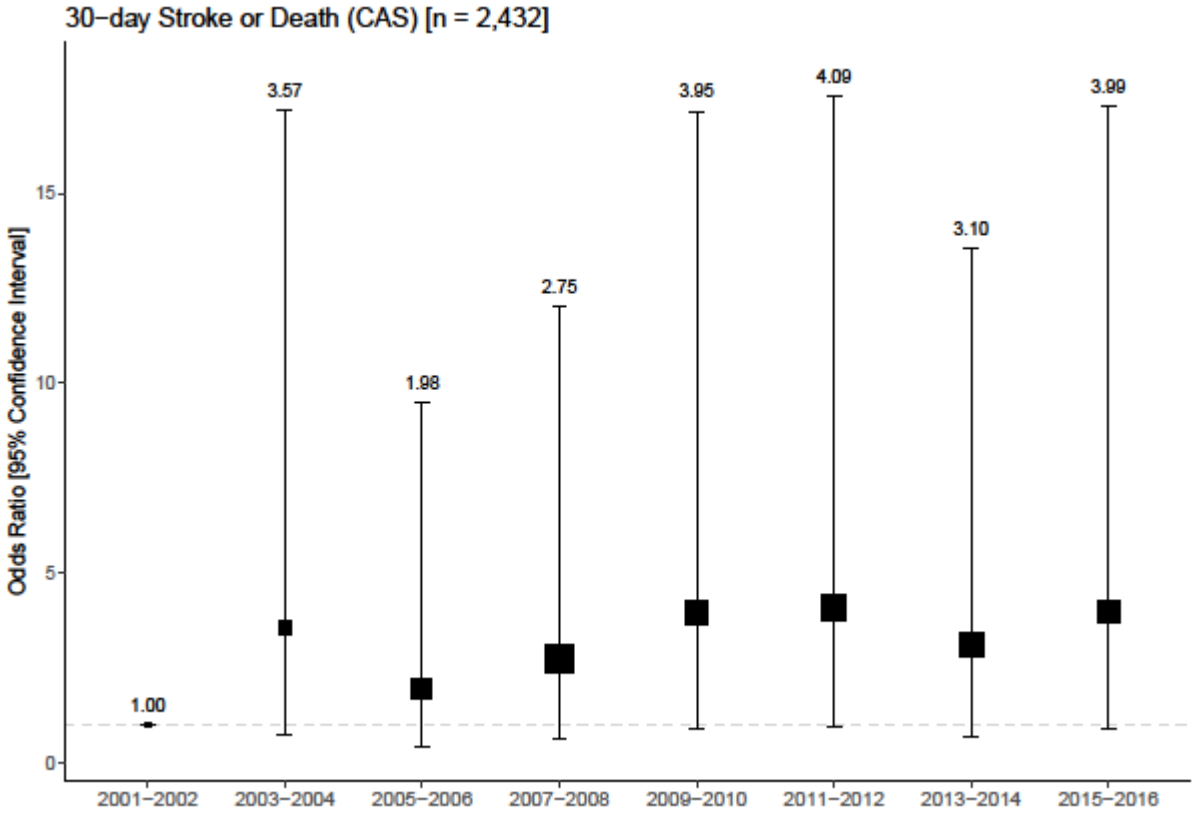

Figure 7.5 (a): Temporal trend in the OR (with 95% CIs) of 30-day stroke/death following CAS in the HES dataset between 2001-2016.

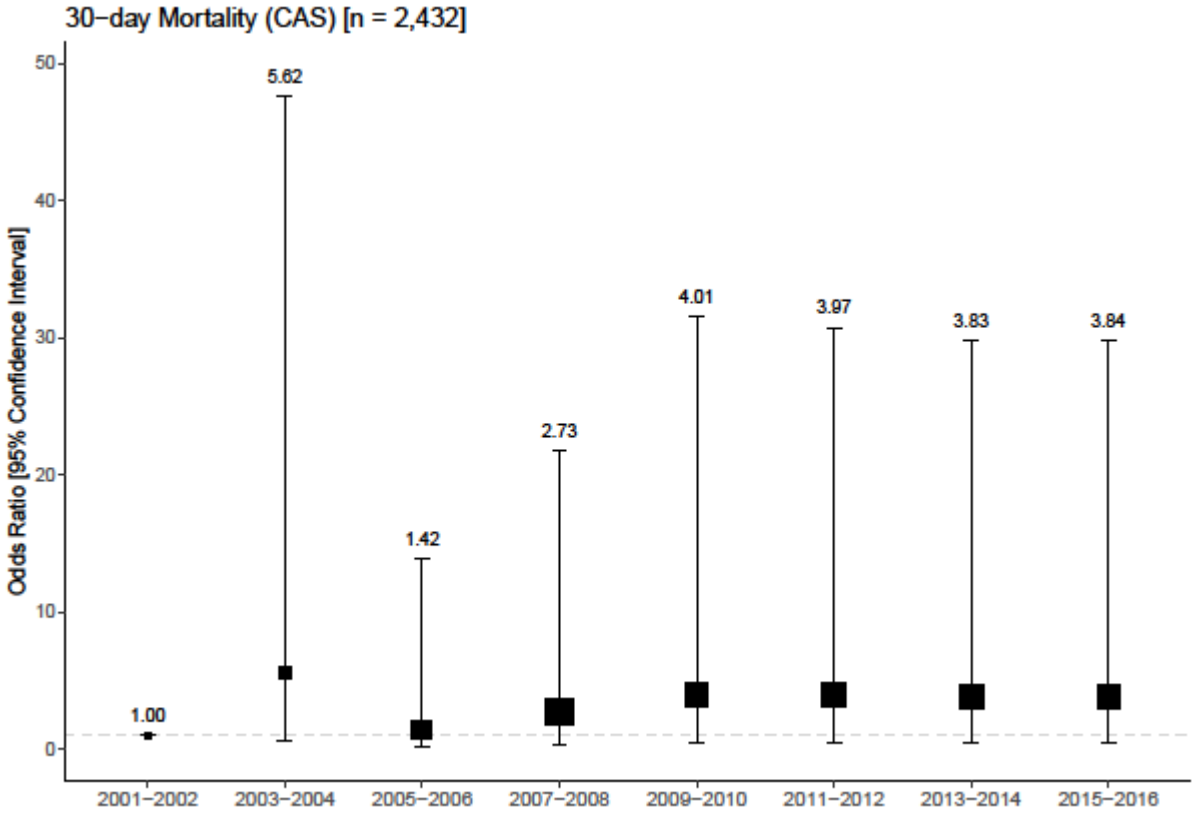

Figure 7.5 (b): Temporal trend in the OR (with 95% CIs) of 30-day mortality following CAS in the HES dataset between 2001-2016.

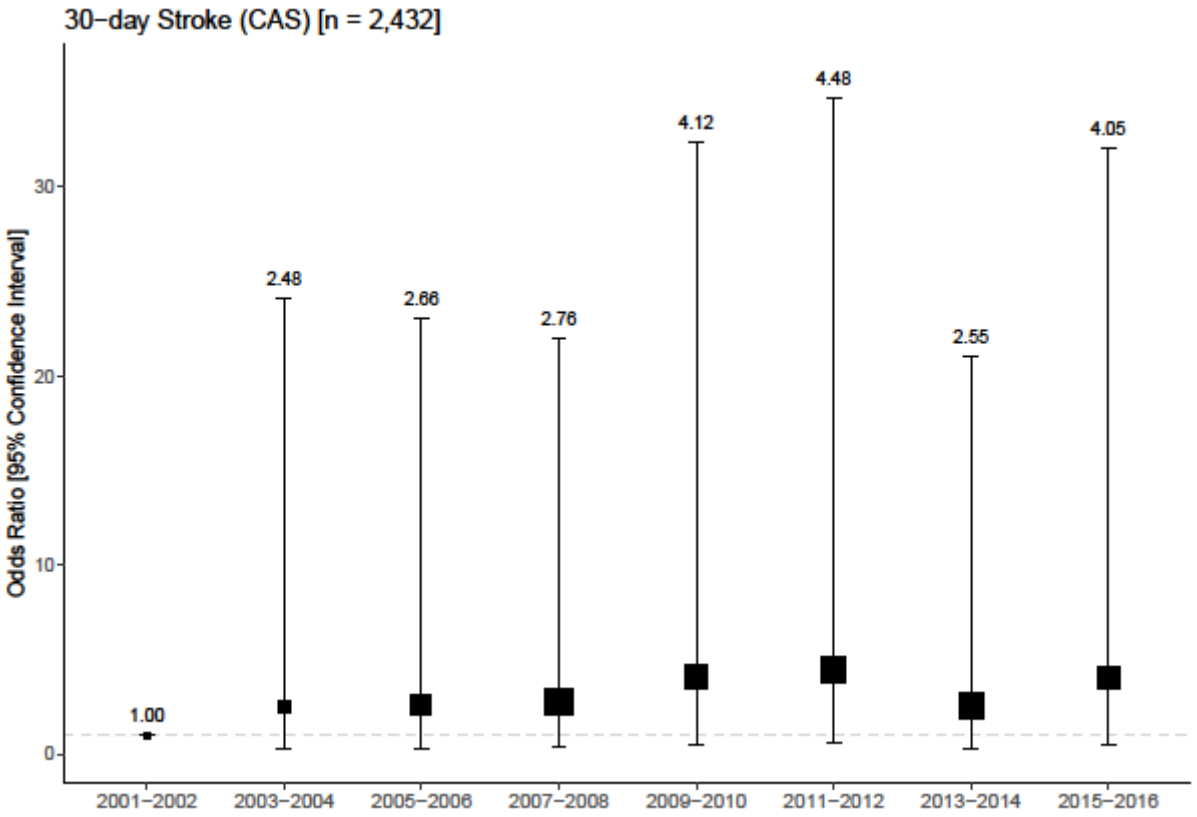

Figure 7.5 (c): Temporal trend in the OR (with 95% CIs) of 30-day stroke following CAS in the HES dataset between 2001-2016.

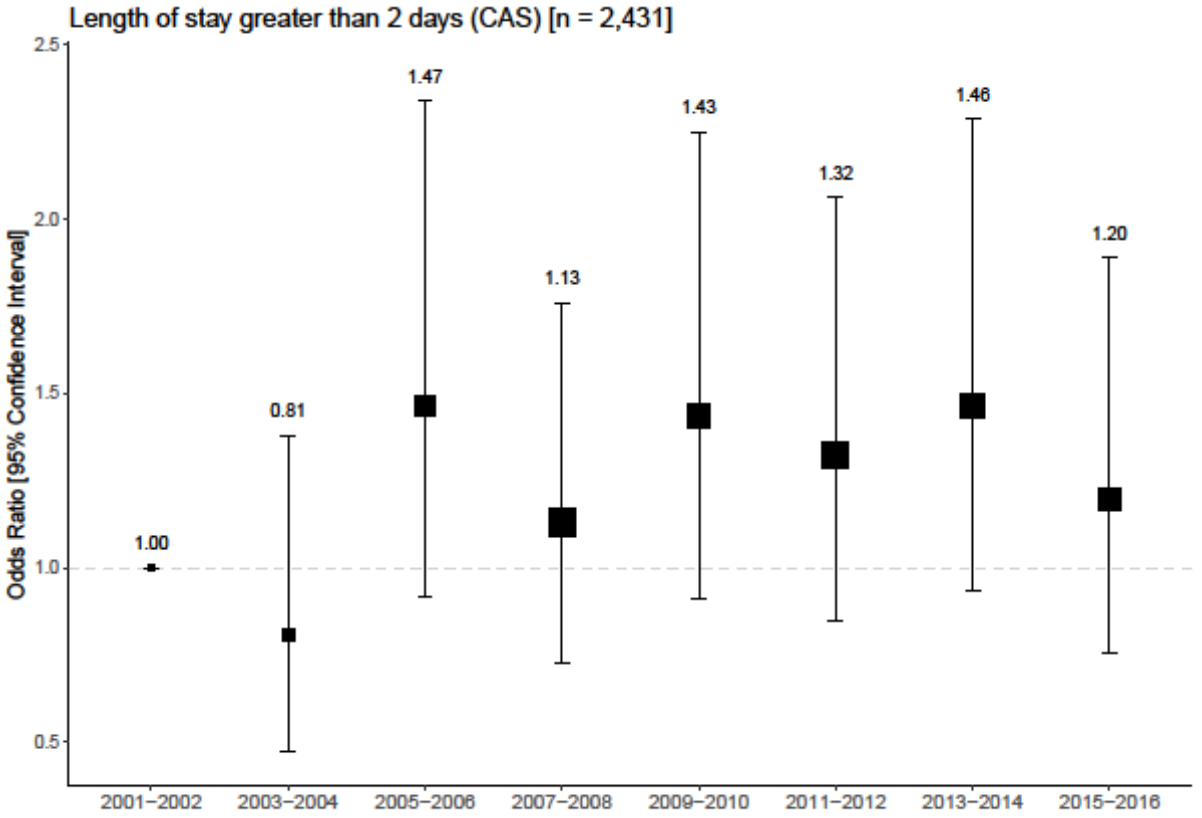

Figure 7.6: Temporal trend in the OR (with 95% CIs) of LOS greater than 2 days following CAS in the HES dataset between 2001-2016.

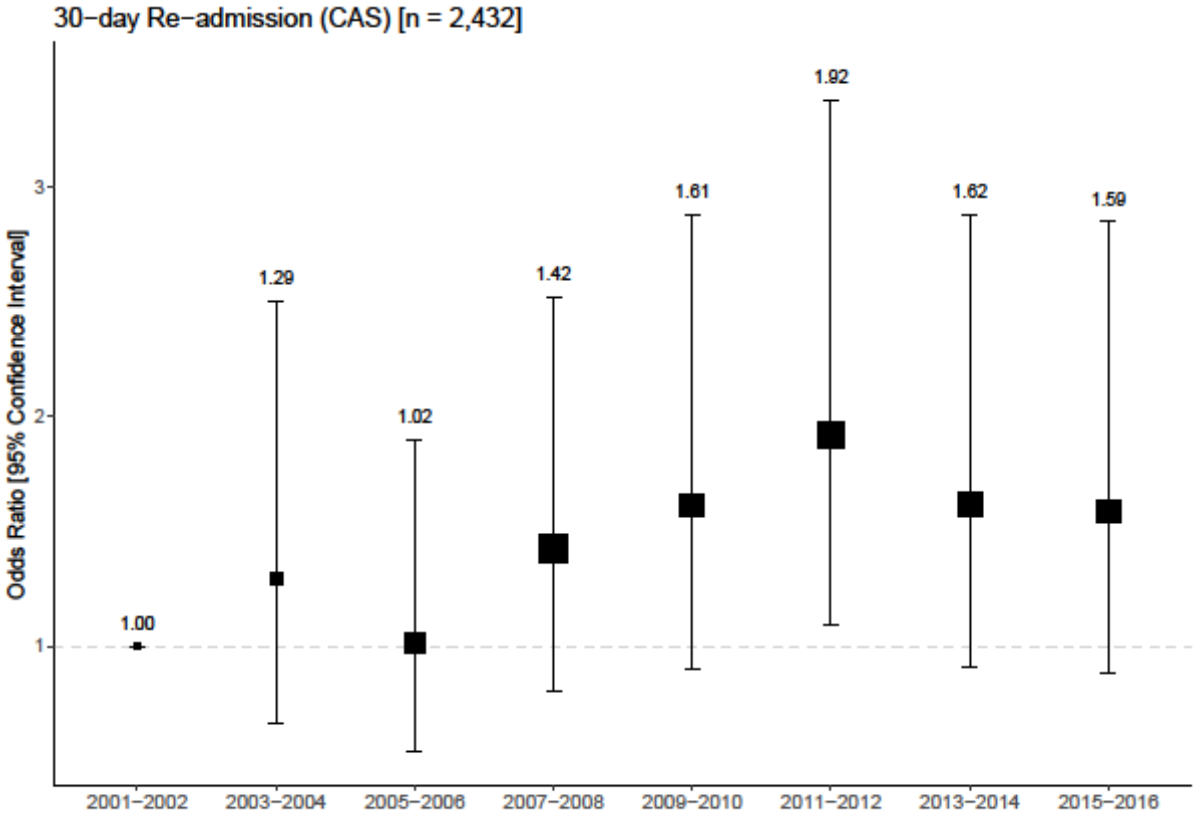

Figure 7.7: Temporal trend in the OR (with 95% CIs) of 30-day re-admission following CAS in the HES dataset between 2001-2016.

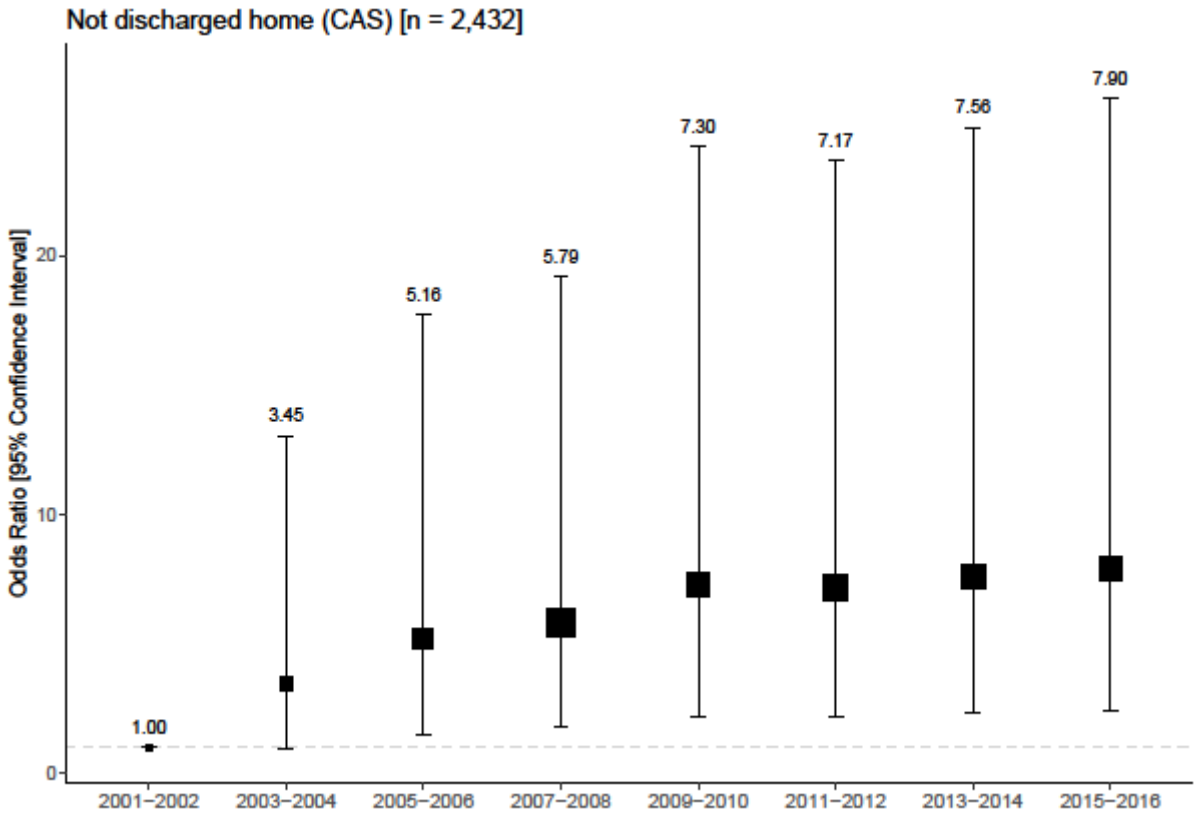

Figure 7.8: Temporal trend in the OR (with 95% CIs) of not being discharged home following CAS in the HES dataset between 2001-2016.

CEA Procedural Outcomes: Regional Trends

East of England and the North East had the lowest risk of procedural stroke/death and stroke (Figures 7.9 (a) and 7.9 (c)) but there was no significant regional variation in procedural mortality following CEA (Figure 7.9 (b); p=0.32). LOS more than 2 days following CEA (Figure 7.10) was significantly more likely in London and East of England but significantly less likely in the South East and South West (all p<0.0001). Re-admission within 30 days following CEA (Figure 7.11) was least likely in the North East, North West and Yorkshire and Humber but significantly more likely in London and the South West (both p<0.0001). Risk of not being discharged home following CEA (Figure 7.12) was comparable between regions, with the North East having the best outcomes and London having significantly worse outcomes (both p<0.0001).

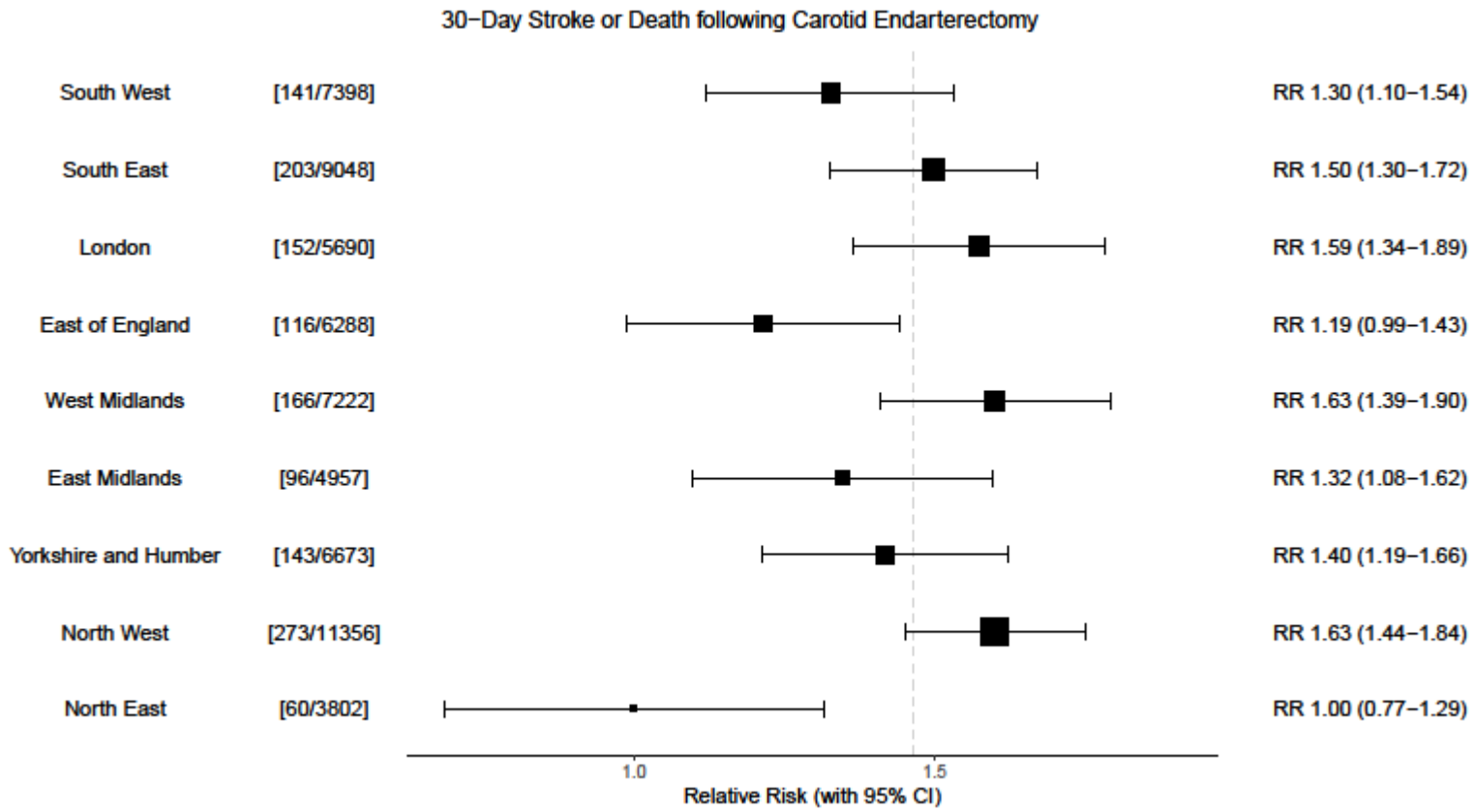

Figure 7.9 (a): Regional trend in the RR (with 95% CIs) of 30-day stroke/death following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

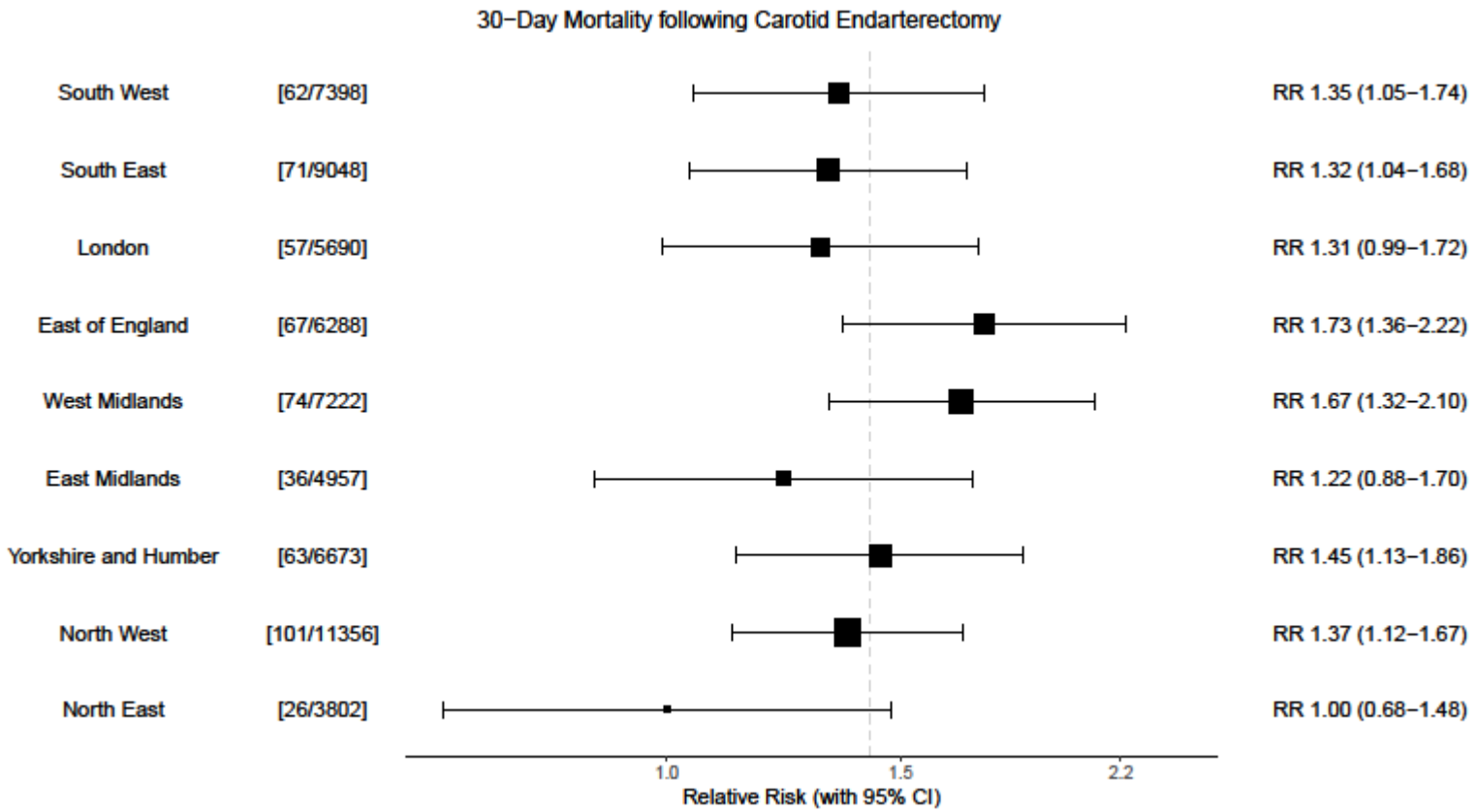

Figure 7.9 (b): Regional trend in the RR (with 95% CIs) of 30-day mortality following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

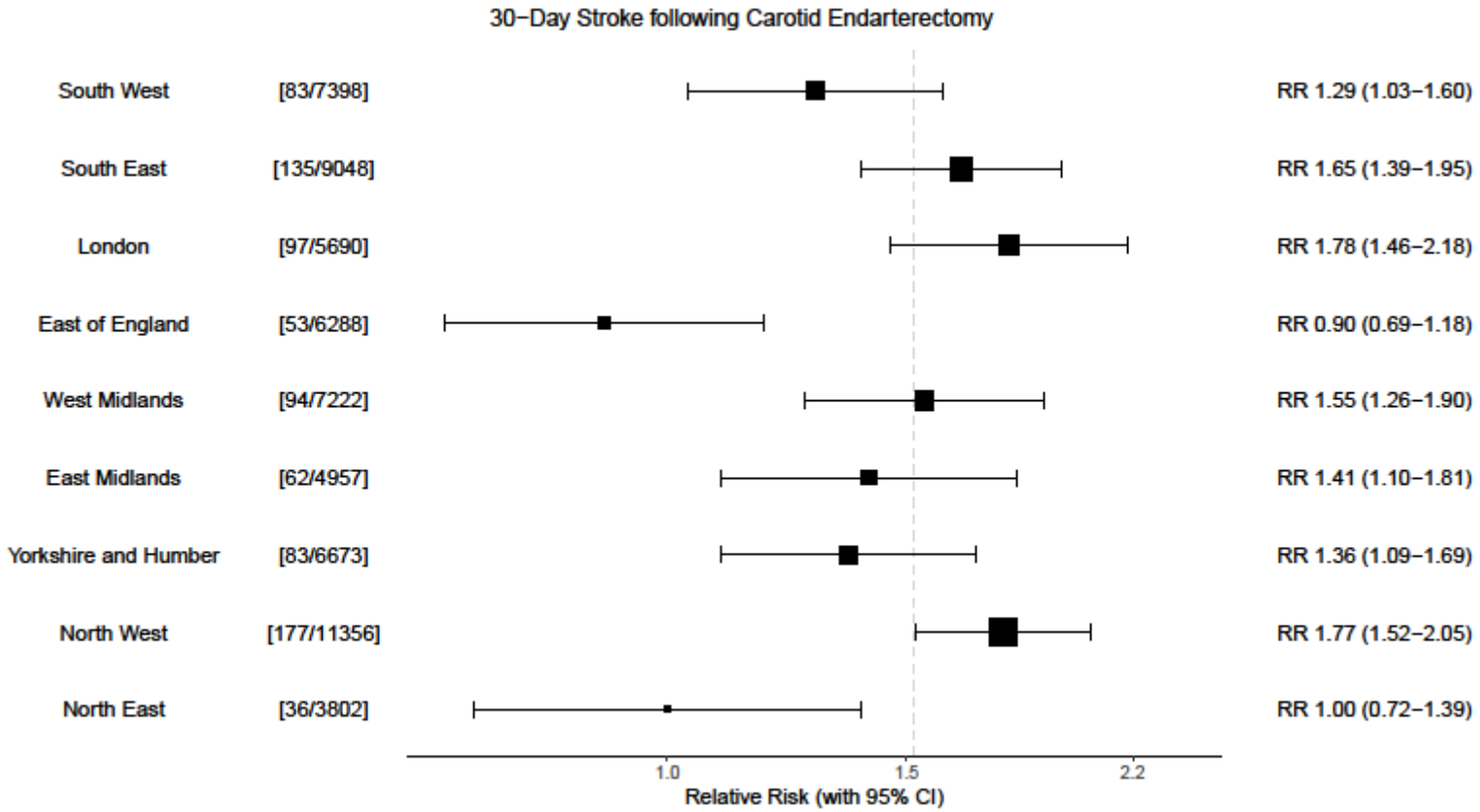

Figure 7.9 (c): Regional trend in the RR (with 95% CIs) of 30-day stroke following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

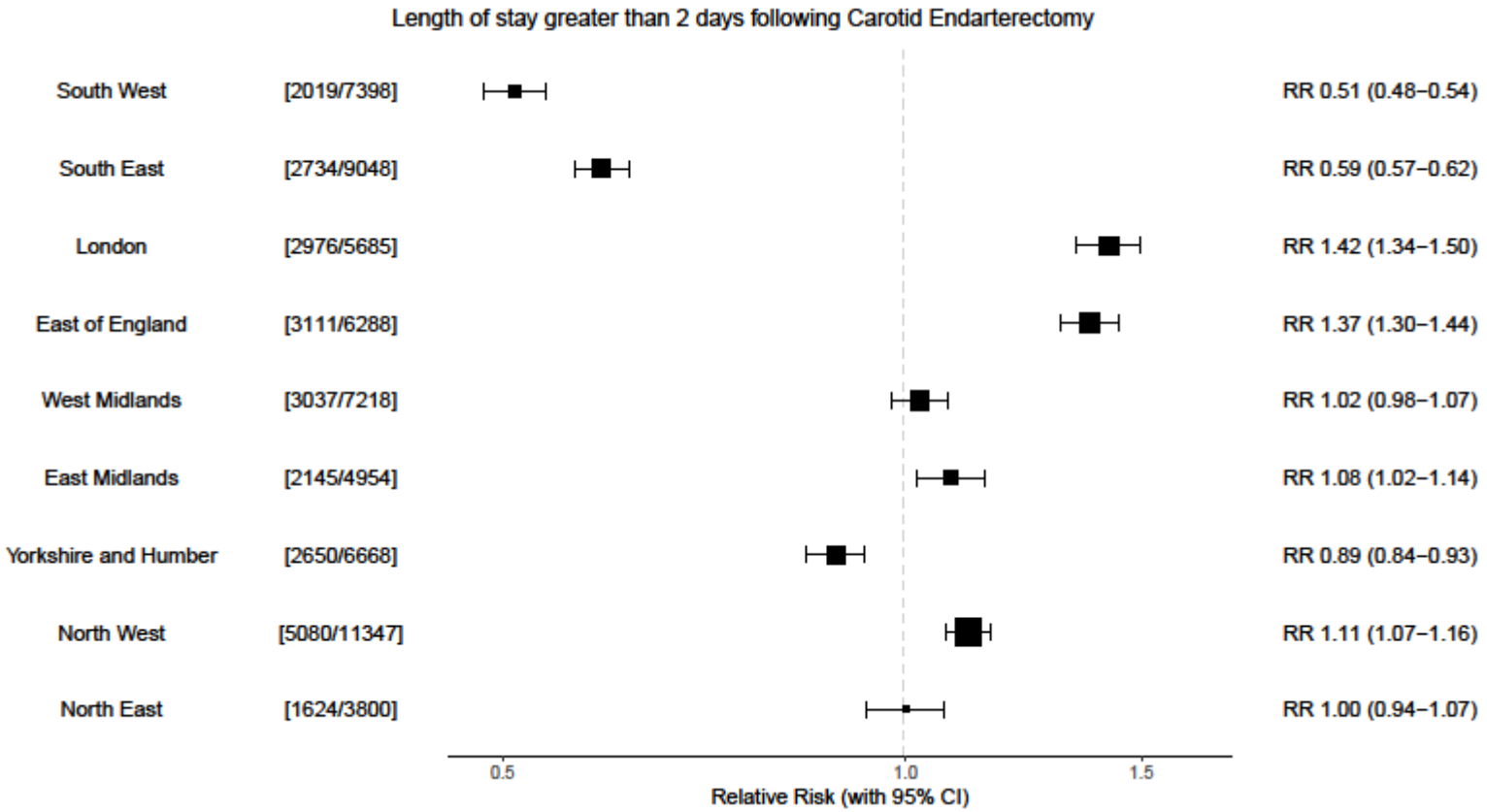

Figure 7.10: Regional trend in the RR (with 95% CIs) of LOS greater than 2 days following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

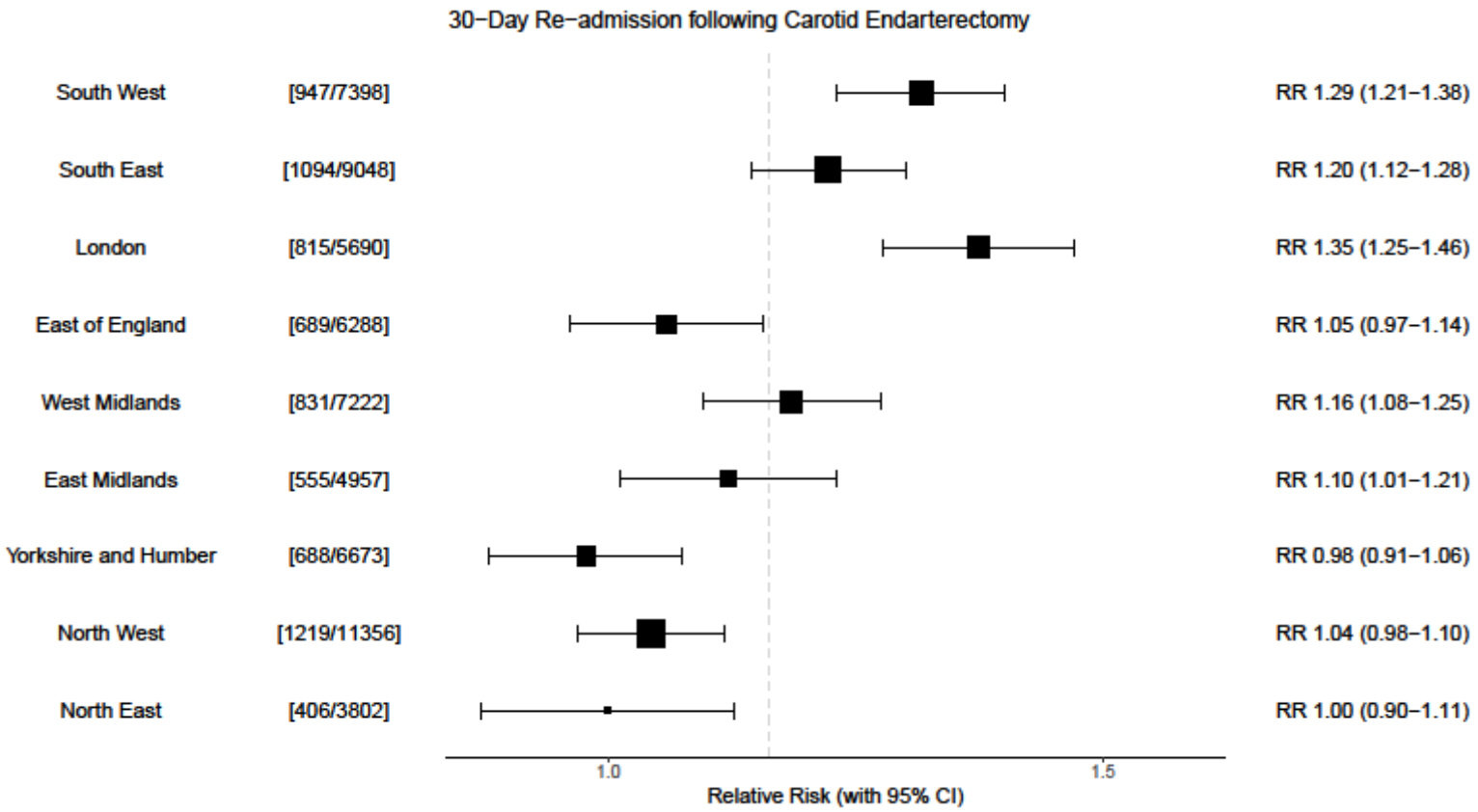

Figure 7.11: Regional trend in the RR (with 95% CIs) of 30-day re-admission following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

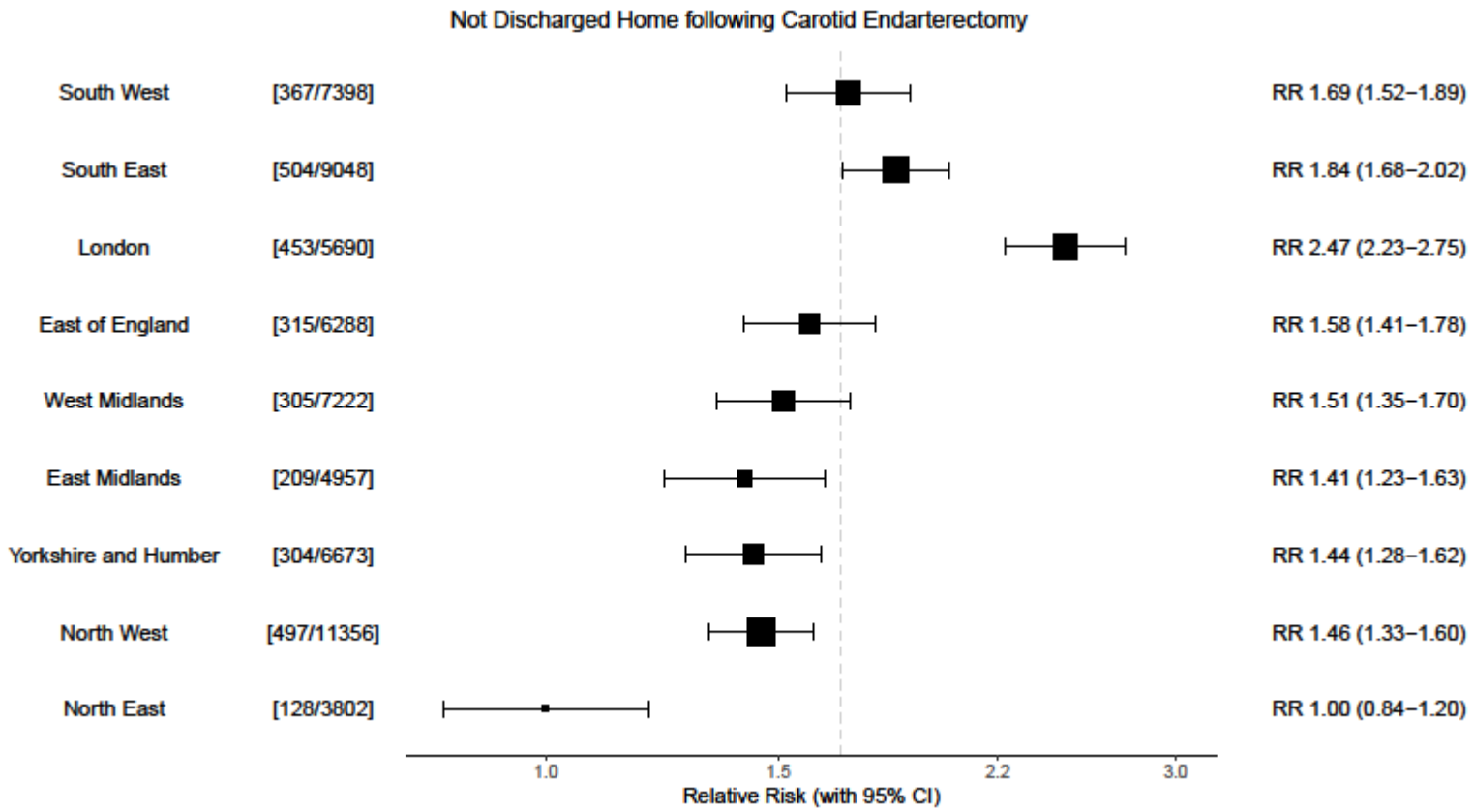

Figure 7.12: Regional trend in the RR (with 95% CIs) of not being discharged home following CEA in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

CAS Procedural Outcomes: Regional Trends

There was no significant regional variation in procedural stroke/death, mortality or stroke following CAS (Figures 7.13 (a), 7.13 (b) and 7.13 (c)). LOS greater than 2 days following CAS (Figure 7.14) was significantly more likely in London ($p<0.0001$) and least likely in the East Midlands and South West. Whilst there was no significant regional variation in re-admission following CAS (Figure 7.15), the risk of not being discharged home (Figure 7.16) was comparable between most regions, with the North East having a significantly lower risk ($p=0.001$) and the South West having the highest risk. These results should be interpreted with caution due to their wide CIs.

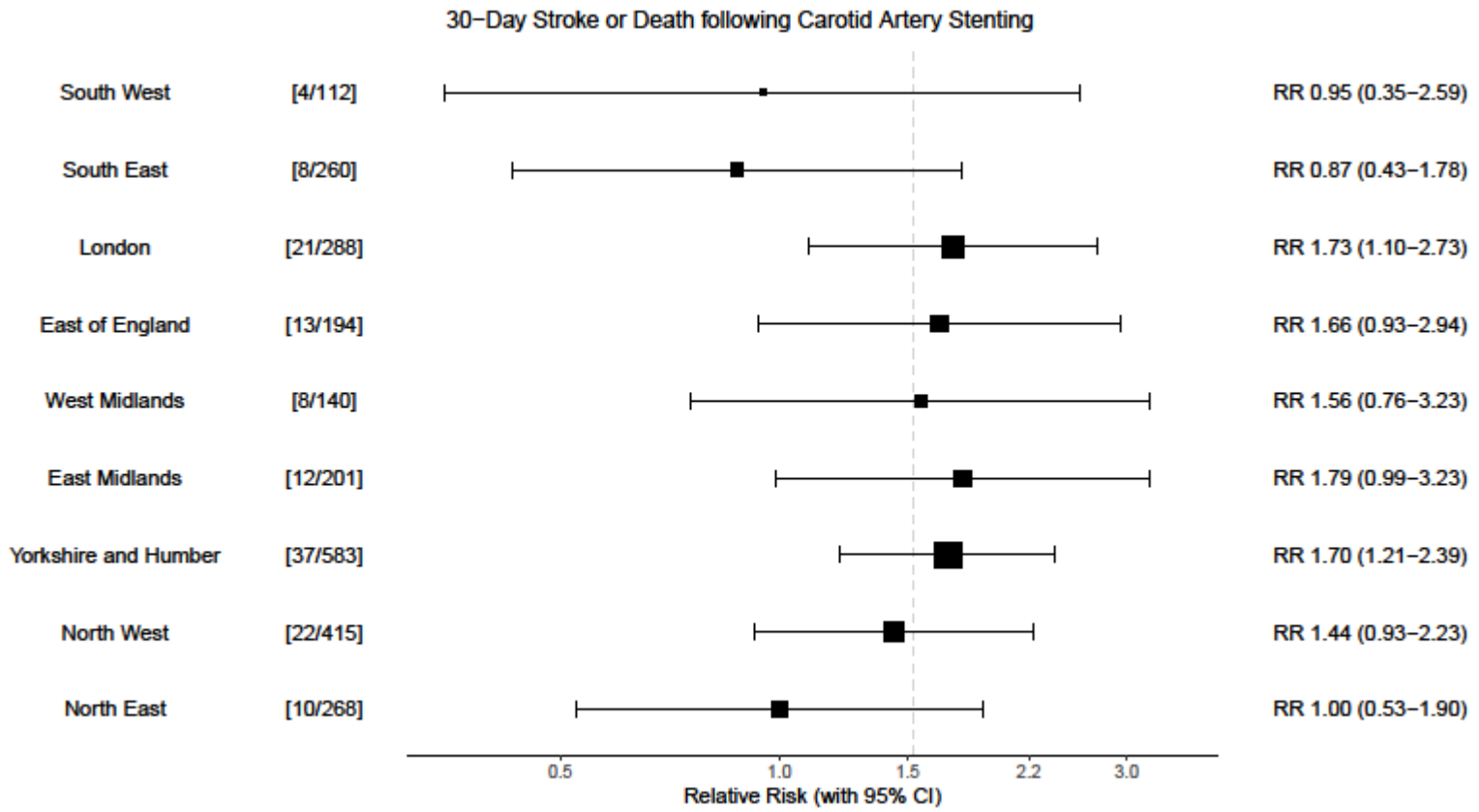

Figure 7.13 (a): Regional trend in the RR (with 95% CIs) of 30-day stroke/death following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

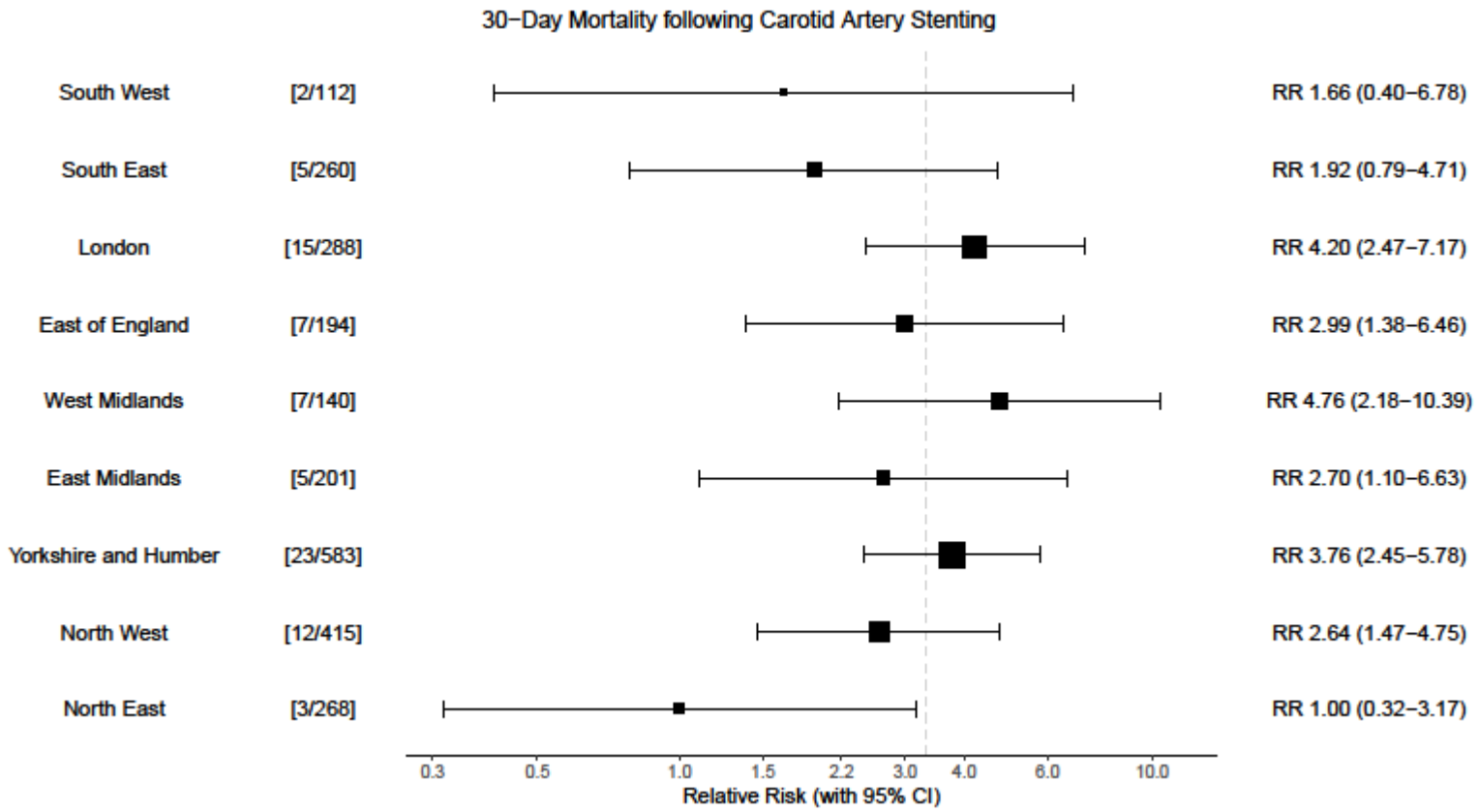

Figure 7.13 (b): Regional trend in the RR (with 95% CIs) of 30-day mortality following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

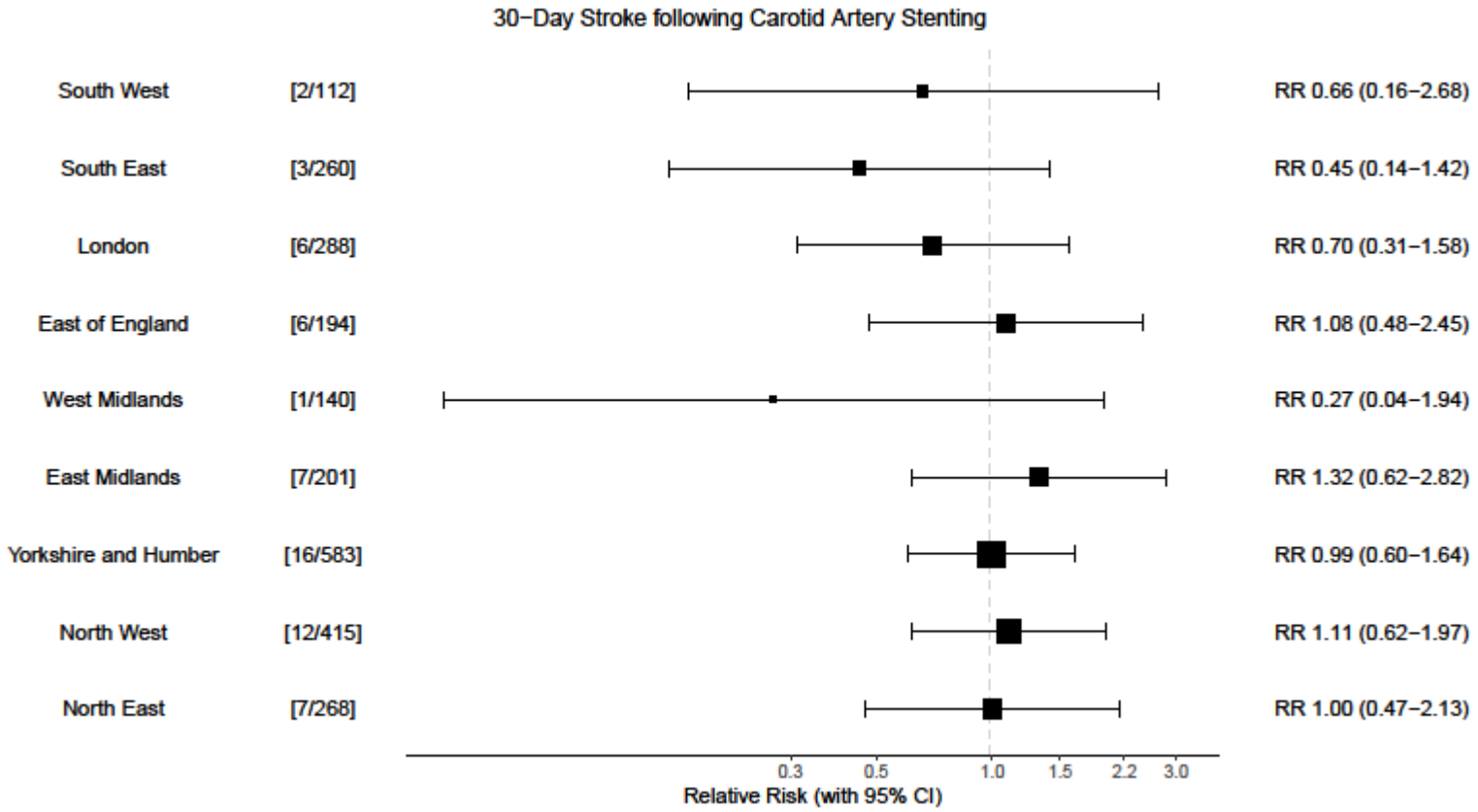

Figure 7.13 (c): Regional trend in the RR (with 95% CIs) of 30-day stroke following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

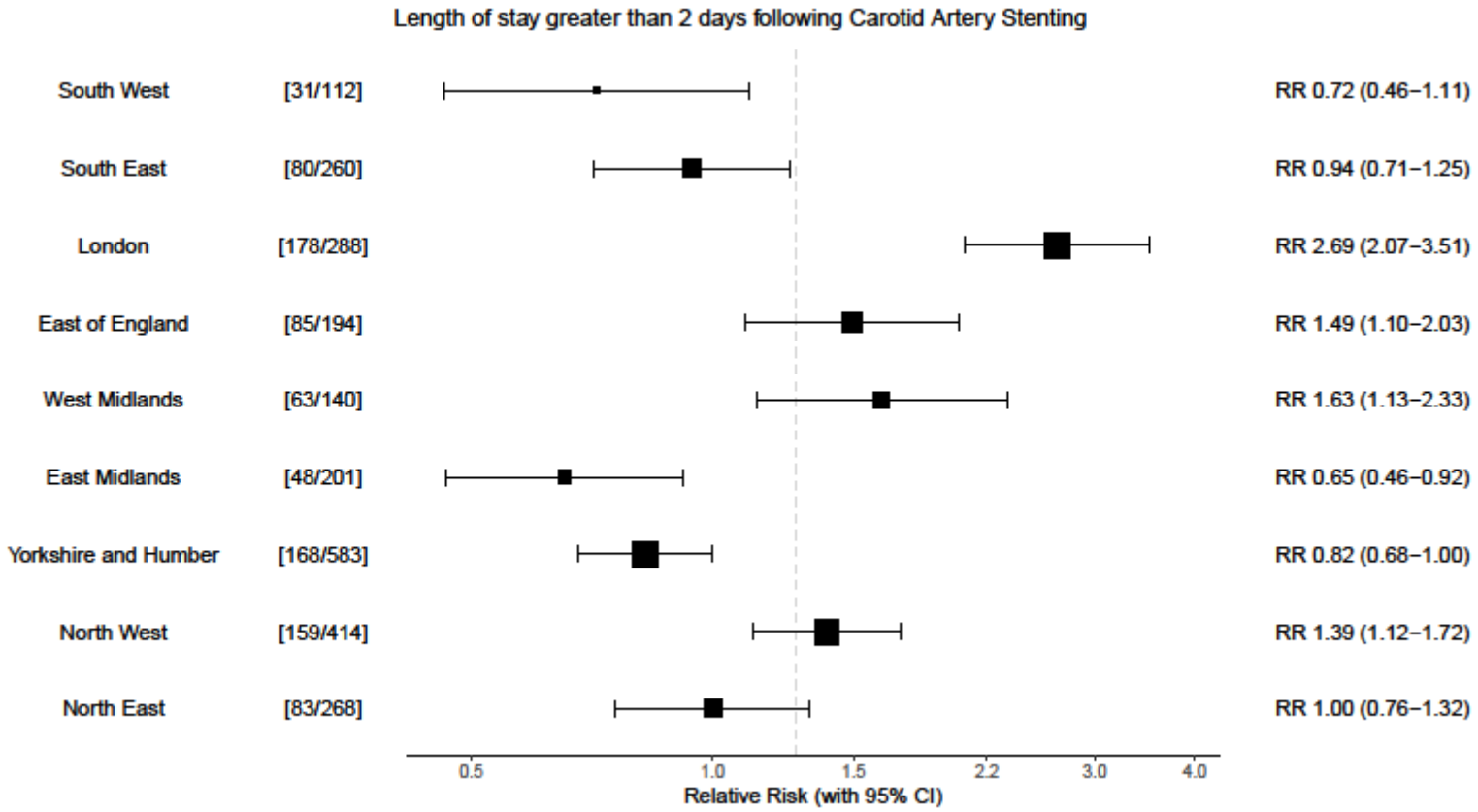

Figure 7.14: Regional trend in the RR (with 95% CIs) of LOS greater than 2 days following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

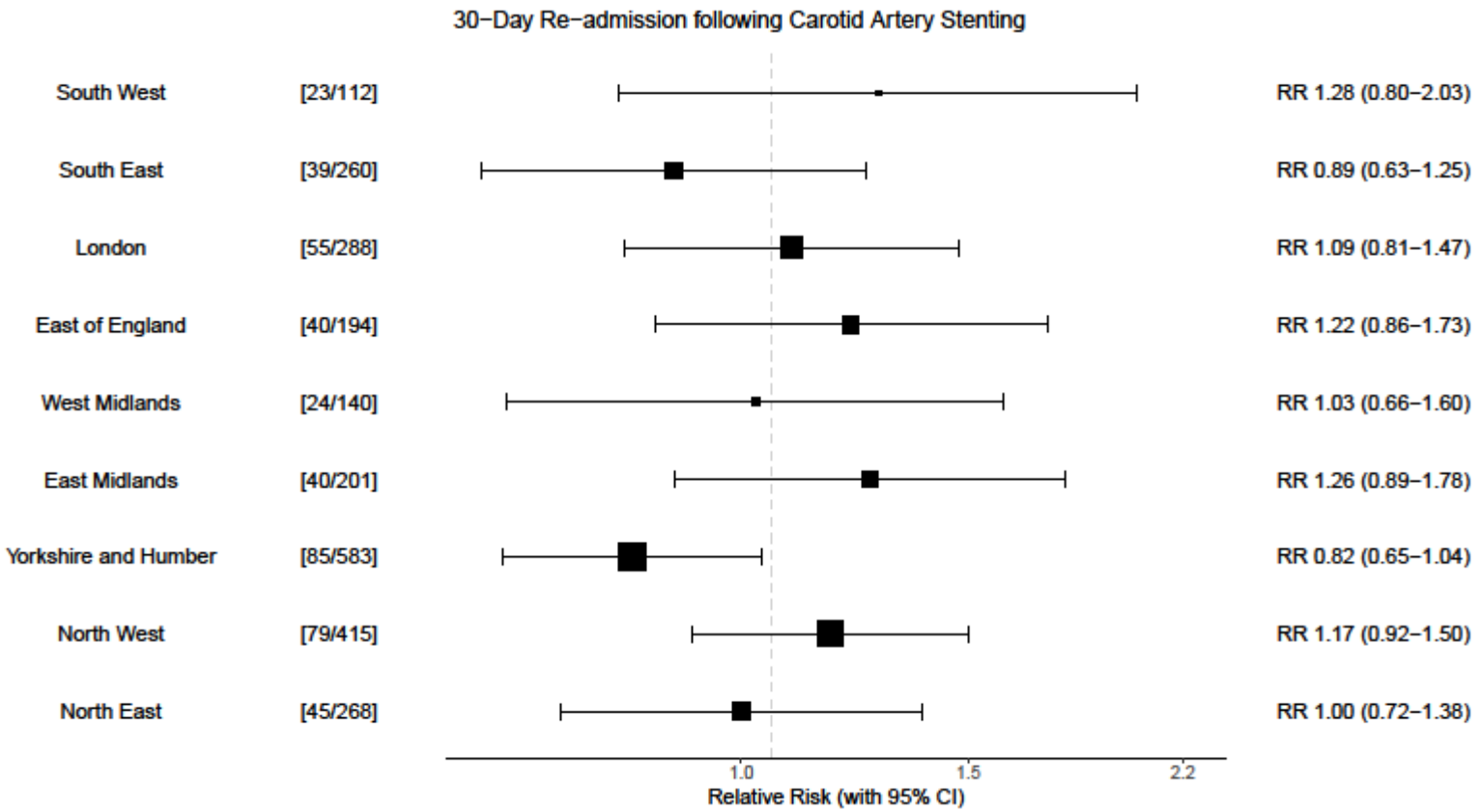

Figure 7.15: Regional trend in the RR (with 95% CIs) of 30-day re-admission following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

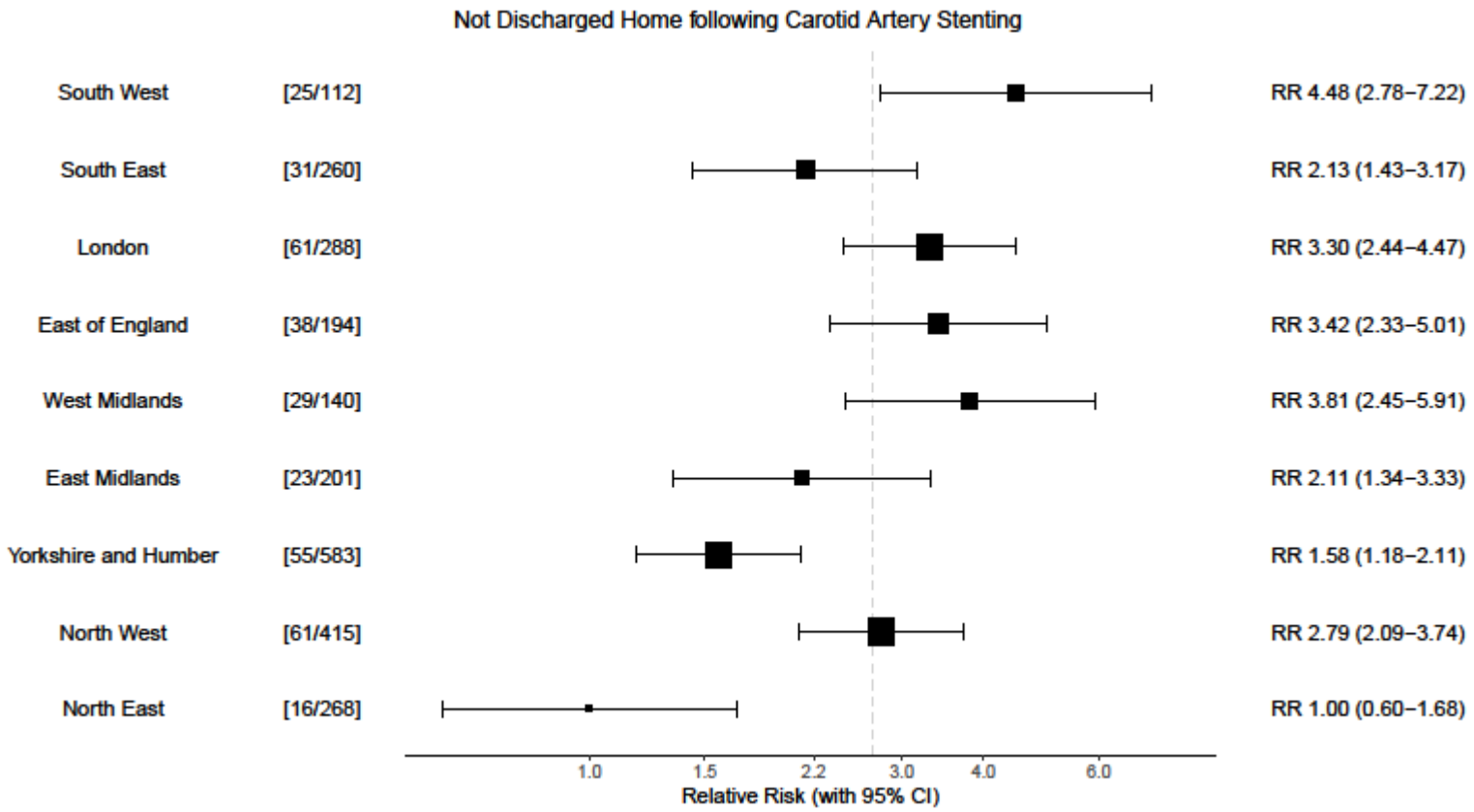

Figure 7.16: Regional trend in the RR (with 95% CIs) of not being discharged home following CAS in the HES dataset between 2001-2016. The dotted line represents the pooled, weighted average.

Long-Term Outcomes

Whilst 20% and 25% of patients had died at 5 years following CEA and CAS respectively, the 5-year stroke rate was less than 10% for both procedures (Figures 7.17 and 7.19).

There was significantly higher event-free probability for mortality and stroke at 30 days and annually from 1-5 years (all $p<0.0001$) following CEA compared to CAS (Figures 7.17 and 7.19). This was sustained at 1, 2, 3, 4 and 5 years (all $p<0.0001$) when the peri-procedural period was excluded (Figures 7.18 and 7.20) but the absolute difference between CEA and CAS was reduced.

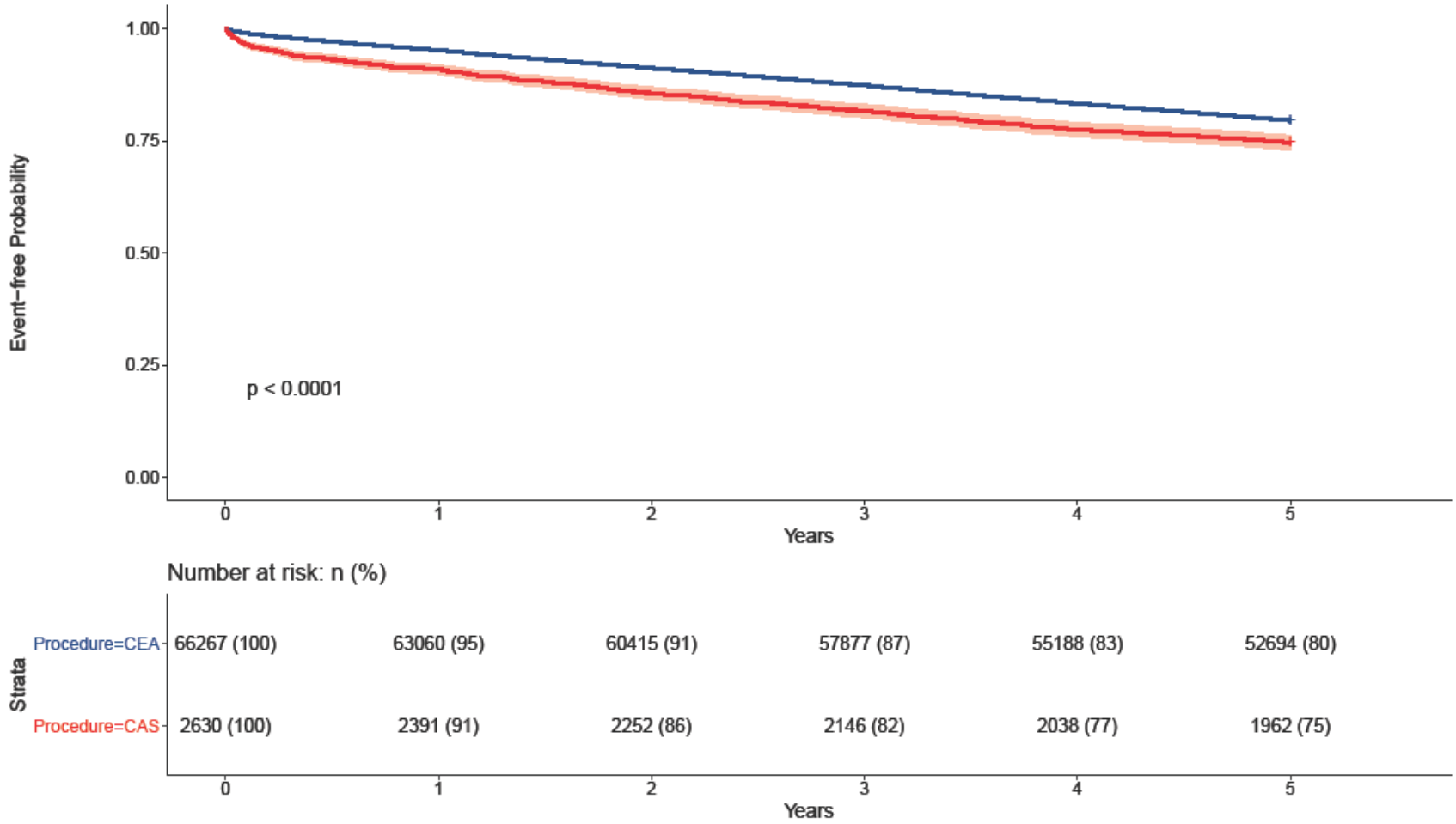

Figure 7.17: Kaplan-Meier curve (with 95% CIs) comparing mortality up to 5 years following CEA and CAS. Mortality was significantly lower in the CEA group compared to patients undergoing CAS at 30 days, 1 year, 2 years, 3 years, 4 years and 5 years (all p<0.0001). Comparisons performed using the log-rank test.

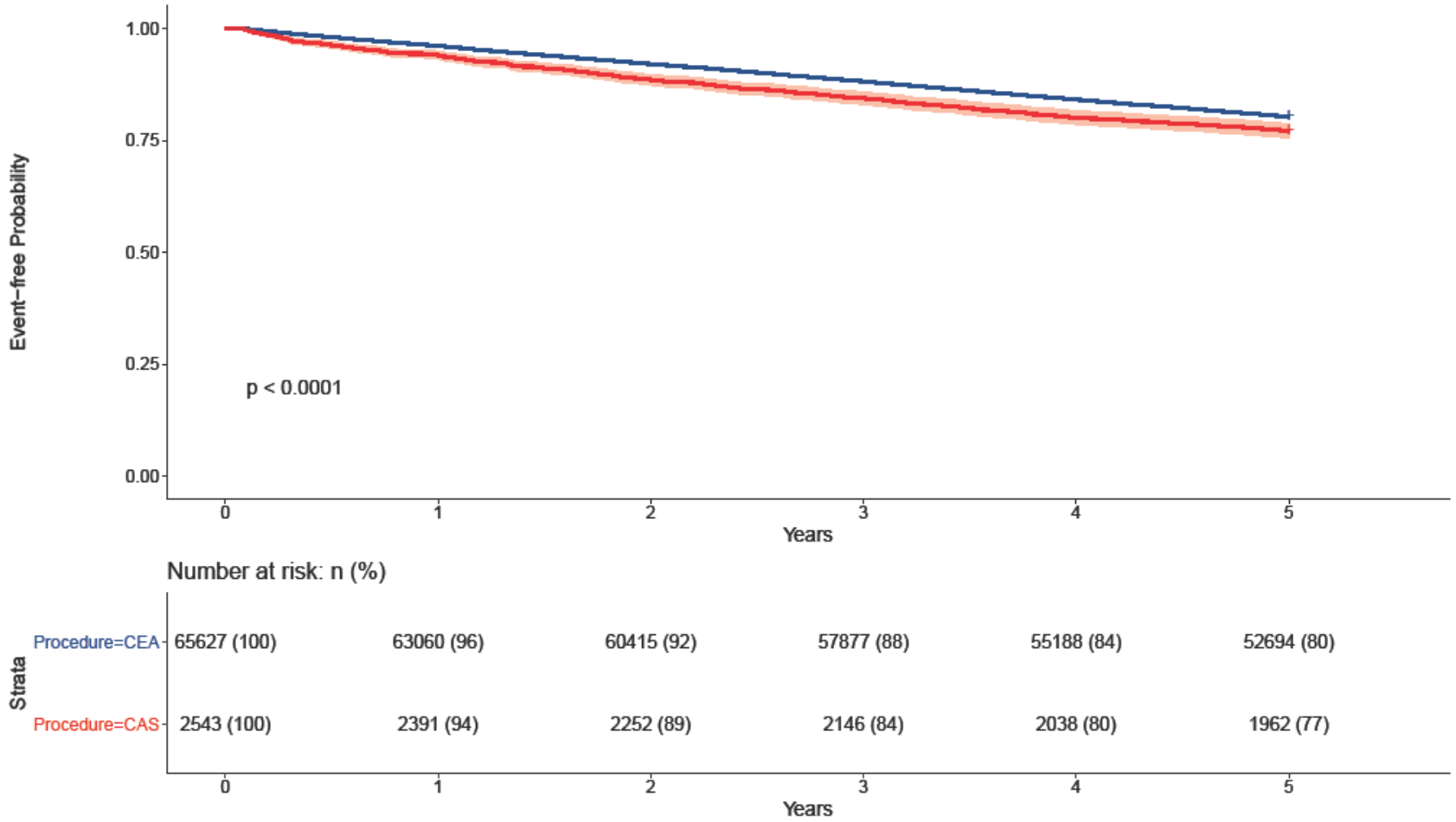

Figure 7.18: Kaplan-Meier curve (with 95% CIs) comparing mortality up to 5 years following CEA and CAS, excluding events up to 30 days post-procedure. Mortality was significantly lower in the CEA group compared to patients undergoing CAS at 1 year, 2 years, 3 years, 4 years and 5 years (all p<0.0001). Comparisons performed using the log-rank test.

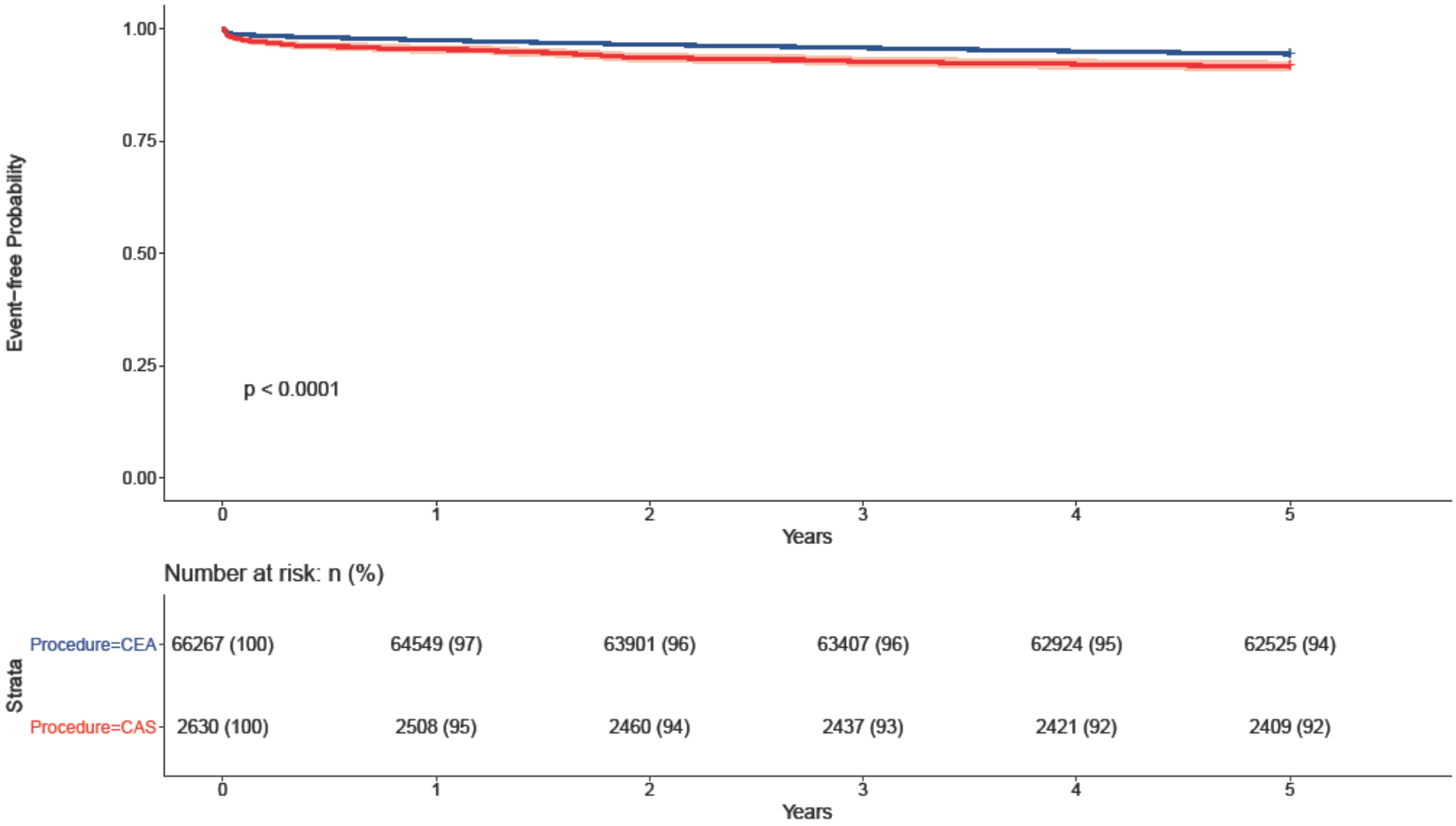

Figure 7.19: Kaplan-Meier curve (with 95% CIs) comparing strokes up to 5 years following CEA and CAS. Stroke rate was significantly lower in the CEA group compared to patients undergoing CAS at 30 days, 1 year, 2 years, 3 years, 4 years and 5 years (all p<0.0001). Comparisons performed using the log-rank test.

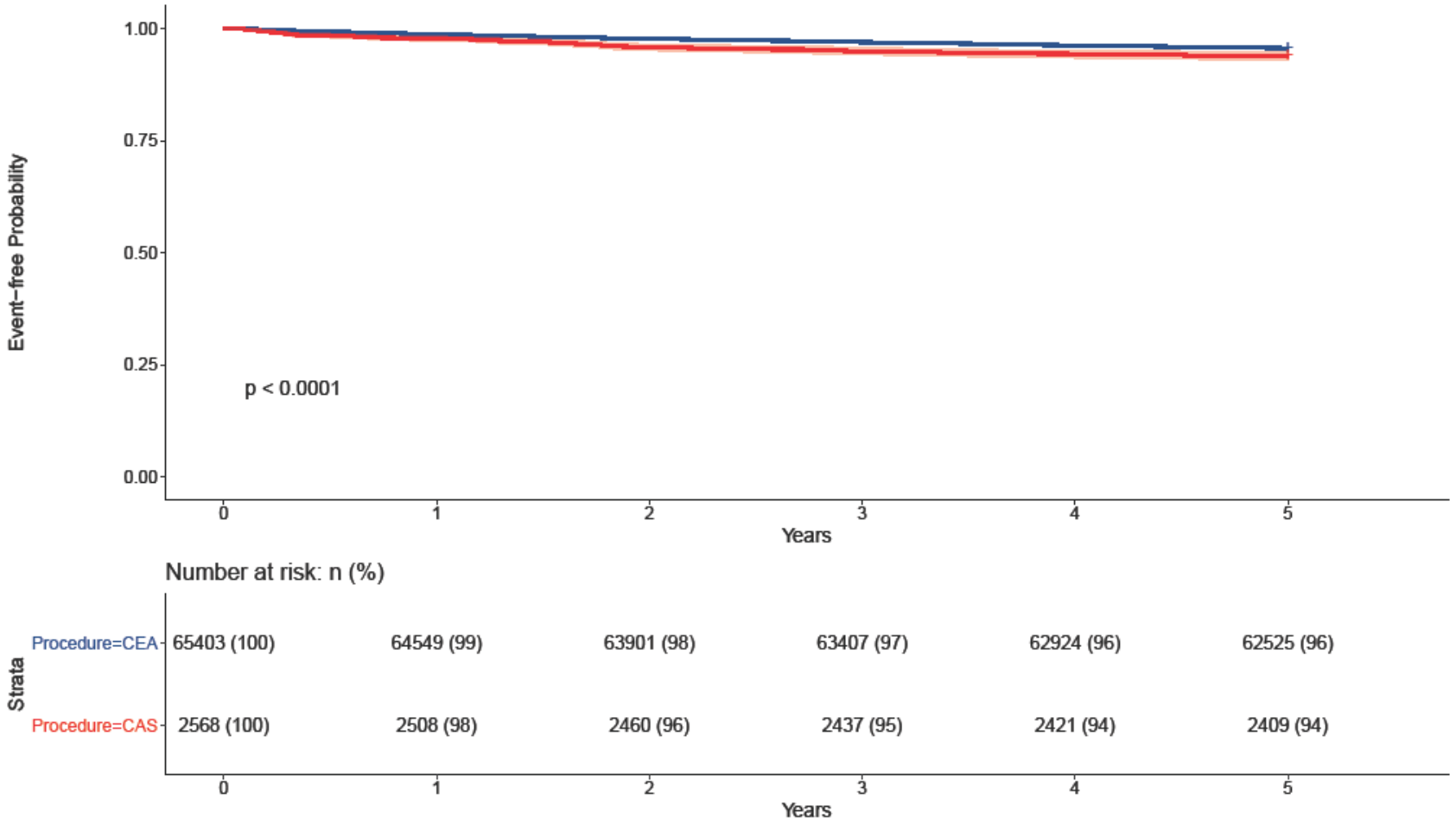

Figure 7.20: Kaplan-Meier curve (with 95% CIs) comparing strokes up to 5 years following CEA and CAS, excluding events up to 30 days post-procedure. Stroke rate was significantly lower in the CEA group compared to patients undergoing CAS at 1 year, 2 years, 3 years, 4 years and 5 years (all p<0.0001). Comparisons performed using the log-rank test.

Predictors of Adverse Long-Term CEA Outcomes

Results from multivariate Cox regression analyses are presented in Tables 7.11 and 7.12 that identified factors associated with adverse long-term CEA outcomes.

CHF, PVD, DM, CRF and prior stroke were associated with adverse long-term CEA outcomes whilst female gender appeared to be protective (Tables 7.11 and 7.12). Increased deprivation was associated with increased long-term stroke risk following CEA whilst non-White ethnicity was associated with reduced long-term stroke risk (Table 7.12). Age 60 years and above was associated with reduced long-term mortality following CEA but increased long-term stroke risk (Tables 7.11 and 7.12).

Table 7.11: Factors associated with 5-year risk of mortality following CEA. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	HR	95% CI	p-value
Age ≥70 years	39,329 (59.4)	10,514	0.90	0.83-0.99	**p=0.022**
Age 60-69 years	18,877 (28.5)	2,493	0.90	0.82-0.99	**p=0.025**
Female	21,653 (32.7)	4,286	0.95	0.91-0.98	**p=0.006**
Prior Stroke	17,770 (26.8)	4,266	1.09	1.03-1.15	**p=0.001**
Prior Stroke/TIA	31,626 (47.7)	7,061	1.04	0.99-1.09	p=0.141
CHF	2,865 (4.3)	1,302	1.23	1.16-1.30	**p<0.00001**
PVD	7,253 (10.9)	2,136	1.08	1.03-1.14	**p=0.001**
DM	14,137 (21.3)	3,662	1.08	1.04-1.13	**p<0.0001**
CRF	3,305 (5.0)	1,146	1.26	1.18-1.34	**p<0.0001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; HR: Hazard Ratio; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Table 7.12: Factors associated with 5-year risk of stroke following CEA. Baseline comparison for age was less than 60 years and baseline comparison for degree of deprivation was IMD1. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	HR	95% CI	p-value
Age ≥70 years	39,329 (59.4)	2,486	4.06	3.72-4.44	**p<0.0001**
Age 60-69 years	18,877 (28.5)	895	1.90	1.73-2.09	**p<0.0001**
Female	21,653 (32.7)	1,366	0.94	0.91-0.98	**p=0.002**
IMD5	13,192 (20.0)	843	1.24	1.17-1.31	**p<0.00001**
IMD4	13,187 (20.0)	768	1.10	1.04-1.16	**p=0.001**
Non-White	2,497 (4.0)	144	0.72	0.65-0.80	**p<0.00001**
Prior Stroke	17,770 (26.8)	1,091	1.29	1.23-1.36	**p<0.00001**
Prior Stroke/TIA	31,626 (47.7)	1,950	1.00	0.95-1.05	p=0.950
CHF	2,865 (4.3)	216	2.09	1.96-2.22	**p<0.00001**
IHD	20,312 (30.7)	1,346	1.23	1.18-1.28	**p<0.00001**
PVD	7,253 (10.9)	508	1.41	1.34-1.48	**p<0.00001**
HTN	44,997 (67.9)	2,707	0.94	0.90-0.98	**p=0.002**
DM	14,137 (21.3)	1,025	1.24	1.19-1.29	**p<0.00001**
CRF	3,305 (5.0)	212	1.30	1.22-1.38	**p<0.00001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; DM: Diabetes Mellitus; HR: Hazard Ratio; HTN: Hypertension; IHD: Ischaemic Heart Disease; IMD: Index of Multiple Deprivation; PVD: Peripheral Vascular Disease; TIA: Transient Ischaemic Attack.

Predictors of Adverse Long-Term CAS Outcomes

Results from multivariate Cox regression analyses are presented in Tables 7.13 and 7.14 that identified factors associated with adverse long-term CAS outcomes.

Stroke prior to CAS was associated with all adverse long-term outcomes (Tables 7.13 and 7.14) but age 60 years and above was associated with increased long-term stroke risk (Table 7.14) and reduced long-term mortality (Table 7.13). Non-White ethnicity was associated with increased long-term mortality (Table 7.13) whilst CHF and CRF were associated with increased long-term stroke risk following CAS (Table 7.14).

Table 7.13: Factors associated with 5-year risk of mortality following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	HR	95% CI	p-value
Age ≥70 years	1,224 (46.7)	421	0.66	0.52-0.85	**p=0.001**
Age 60-69 years	822 (31.4)	160	0.75	0.57-0.99	**p=0.044**
Female	904 (34.4)	229	0.99	0.84-1.17	p=0.947
Non-White	135 (5.4)	31	1.79	1.24-2.60	**p=0.002**
Prior Stroke	750 (28.5)	222	1.47	1.16-1.87	**p=0.002**
Prior Stroke/TIA	1,303 (49.5)	356	0.95	0.76-1.20	p=0.675

Abbreviations – CI: Confidence Interval; HR: Hazard Ratio; TIA: Transient Ischaemic Attack.

Table 7.14: Factors associated with 5-year risk of stroke following CAS. Baseline comparison for age was less than 60 years. Statistically significant values are highlighted in bold.

Factor	Patients (n, %)	Events (n)	HR	95% CI	p-value
Age ≥70 years	1,224 (46.7)	116	2.30	1.80-2.94	**p<0.0001**
Age 60-69 years	822 (31.4)	62	1.32	1.01-1.74	**p=0.045**
Female	904 (34.4)	67	1.09	0.92-1.28	p=0.321
Prior Stroke	750 (28.5)	64	1.39	1.10-1.76	**p=0.006**
Prior Stroke/TIA	1,303 (49.5)	112	0.97	0.78-1.21	p=0.780
CHF	196 (7.5)	26	1.69	1.33-2.15	**p<0.00001**
CRF	150 (5.7)	12	1.73	1.34-2.24	**p<0.00001**

Abbreviations – CHF: Congestive Heart Failure; CI: Confidence Interval; CRF: Chronic Renal Failure; HR: Hazard Ratio; TIA: Transient Ischaemic Attack.

Discussion

This study has shown that IHD, PVD, DM, CRF, age 70 years and above and non-White ethnicity were associated with significantly increased risk of adverse CEA procedural outcomes. Increased deprivation was associated with significantly increased risk of procedural mortality and prolonged LOS following CEA but did not affect CAS outcomes whilst non-White ethnicity was associated with significantly prolonged LOS following CAS. Prior stroke and CHF were associated with adverse CEA and CAS procedural outcomes whereas female gender was associated with secondary outcomes. There was overlap between risk factors for adverse procedural and long-term CEA and CAS outcomes. Since 2001, procedural stroke/death, mortality and LOS improved whilst re-admission worsened following CEA. Procedural stroke/death, mortality, stroke and LOS did not change over time following CAS but risk of not being discharged home significantly worsened. There was also regional variation in CEA and CAS procedural outcomes. Whilst these findings may improve patient selection for these interventions, further investigation is required to understand reasons for worsening of some CEA and CAS procedural outcomes over time, their regional variation and differences in long-term outcomes post-procedurally.

Trends in Procedural Outcomes: Patient Characteristics

Procedural stroke/death and stroke rates following CEA in this study (2.2% and 1.3% respectively) are comparable to the figures of 2.0% and 1.7% published in the NVR annual report.[97] Moreover, our median LOS following CEA is identical to the nationally published figure.[97] This provides validity to our findings as they support results from a registry that represents contemporary UK vascular practice with a case-ascertainment rate of 96% in 2018.[97]

However, our 30-day re-admission rate following carotid intervention is higher than the national figure of 4.4% following CEA.[97] This is likely due to re-admissions in our patients that may not have been directly related to CEA and CAS (e.g. lower respiratory tract infection). When considering re-admissions directly related to the procedure, our figure of 4.0% is comparable to UK practice.[97]

Our finding that IHD, CHF, PVD, DM, CRF and prior stroke were all associated with increased risk of CEA and CAS procedural complications is supported by the literature. DM has been shown to predict significantly worse CEA and CAS outcomes[12, 49-55] whilst smaller studies reported non-significant adverse outcomes in diabetic than non-diabetic patients.[6, 56-59] PVD was also associated with significantly worse CEA and CAS outcomes[6, 15, 50, 51] whilst IHD increased CEA and CAS procedural risk.[15, 51, 60] However, this was not always statistically significant, probably due to the lack of power of these small studies.[6, 12, 50, 61] CRF also predicted significantly worse CEA and CAS outcomes[49, 63-69, 73] and was most pronounced in patients with severe CRF (including end-stage renal disease)[70-72] whilst symptomatic patients undergoing CEA and CAS were at increased risk of procedural stroke/death, stroke (major and minor) and stroke/death/MI compared to asymptomatic patients in CREST-1.[98] Our results provide increased power to the surgical literature and highlight important comorbidities that should be considered when assessing suitability of patients for carotid intervention to optimise procedural outcomes.

Non-White ethnicity was significantly associated with adverse CEA outcomes but only prolonged LOS following CAS in our study. This is broadly consistent with various studies that have reported increased rates of procedural stroke and death in non-White patients undergoing CEA compared to White patients.[35, 38-45] This has been partly attributed to increased rates of DM, HTN, CRF, previous stroke, IHD and CHF in non-White compared to White patients.[40, 42-47] Choi *et al*.[48] reported comparable in-hospital mortality following CAS between

White and non-White patients[48] (similar to our findings), whilst another study[36] found that non-White English adults were significantly more likely to have a prolonged LOS (p=0.003) in a sample of patients undergoing CEA (n=15,996) and CAS (n=632) between 2009-2012. Whilst our findings support the surgical literature, they should be interpreted with caution due to the majority of patients being White ethnicity (96.0% CEA; 94.6% CAS). The small numbers of non-White patients in our study means our results are underpowered to reliably demonstrate meaningful associations between ethnicity and CEA and CAS procedural outcomes. This study has therefore highlighted associations that require further investigation in a larger cohort of different ethnic groups, in a country which has patients from more diverse backgrounds than England.

Our finding that increased deprivation was significantly associated with increased procedural risk of death and LOS following CEA is supported by a study that reported significantly higher in-hospital mortality following carotid intervention in the lowest income quartile compared to the highest.[35] LOS following CEA and CAS in the lowest income quartile was also significantly prolonged compared to the highest ($p<0.0001$).[35] However, no study to date has reported the effect of degree of deprivation on CAS outcomes and our study did not report an association (perhaps due to the smaller numbers of CAS procedures in our cohort). Further analyses are required to better understand the effect of deprivation on CAS outcomes.

Age 70 years and above was associated with significantly increased risk of procedural stroke following CAS. This is in keeping with various RCTs. CREST-1 reported significantly increased procedural risk of stroke/death and stroke following CAS in octogenarians than those aged less than 80 years, even after adjusting for symptom status, stenosis, EPD use and gender.[99] This was driven by increased stroke risk following CAS in patients older than 64 years.[11] SPACE-1[100] reported that the risk of stroke/death significantly increased with age in patients receiving CAS whilst ICSS[101] also found that increasing age predicted adverse

procedural CAS outcomes. Subsequent meta-analyses, with[102] and without[12] data from CREST-1, reported significantly increased procedural risk of stroke/death in patients aged over 70 years following CAS, where the risk was more than double CEA. These meta-analyses did not report an age effect on CEA outcomes, in contrast to our findings[12, 102], and may reflect the different population in our unselected dataset which contrasts to highly selected patients enrolled in RCTs. Our patients are likely to be more co-morbid than those enrolled in RCTs and increasing age may be a marker of increasing comorbidities, explaining why patients aged 70 years and above had adverse CEA procedural outcomes in our dataset.

Female gender was not associated with increased risk of procedural stroke/death or mortality following CEA and CAS. This is supported by registry studies and a systematic review.[13-15] Single-centre, retrospective studies have also not reported significant differences in CEA procedural outcomes by gender.[17-25] However, ACAS, NASCET and ACST-1 reported worse outcomes in females.[2-5, 8] This was more pronounced following CEA in ICSS[9] and following CAS in CREST-1.[10] These findings have also been supported by a meta-analysis[12] and older, small studies.[26-32] However, it seems unlikely that female gender increases CEA and CAS risk. This finding may be due to underpowered subgroup analyses of RCT findings, causing potential statistical artefact. Large registry studies[13, 14], representing routine practice with statistical power, have reported no difference in CEA or CAS procedural outcomes in females versus males and this is supported by our results when examining primary outcomes. Results from large administrative datasets (e.g. HES) may generalise more than RCT findings and provide more clarity regarding the association between gender and CEA and CAS procedural outcomes in contemporary practice.

Trends in Procedural Outcomes: Temporal

Our finding that the odds of procedural stroke/death and mortality following CEA significantly improved with time is supported by other studies.[38, 48, 74-76, 78] This may be due to improved CMT, pre-operative optimisation, advancement in surgical and regional anaesthesia and sub-specialisation of Surgeons leading to increased familiarity and experience with CEA. However, our finding that the procedural stroke rate following CEA has tended to worsen (being statistically significant in 2013-2014) contrasts with another study.[38] A possible explanation for this may be improved coding over time which almost trebled the number of procedural strokes captured between 2001-2002 (n=53) and 2013-2014 (n=156), inflating procedural stroke risk. Furthermore, Matsen *et al.*[38] reported the in-hospital stroke rate whereas we examined 30-day stroke rate. The odds of re-admission within 30 days of CEA significantly worsened before slightly improving. This may be related to LOS following CEA significantly reducing, especially from 2001-2002 until 2009-2010. It appears that, in the early years of our study, patients may have been discharged prematurely following CEA (to improve efficiency of care) resulting in short LOS, but subsequent re-admission. Since 2011-2012, the correct balance appears to have been found between short LOS and decreased re-admission risk.

We did not find temporal improvements in the risk of procedural stroke/death, mortality, stroke or prolonged LOS following CAS in our study. This is similar to Lichtman *et* al.[74] but contrasts with other studies.[48, 74-77] This lack of detectable improvement in CAS outcomes over time is likely due to our study being underpowered. The trend for re-admission also followed a similar pattern to CEA but, was much less exaggerated possibly again due to smaller numbers of CAS procedures. However, we detected significant worsening in the odds of not being discharged home after 2005-2006. Whilst this should be interpreted with caution due to wide CIs, it requires further investigation.

Trends in Procedural Outcomes: Regional

This is the first study that has identified regional variation in CEA and CAS procedural outcomes in England. Whilst there was no regional variation for CEA mortality, the North East was associated with significantly reduced risk of stroke/death and not being discharged home whilst London was associated with increased risk of prolonged LOS, re-admission and not being discharged home following CEA. There was no variation in procedural stroke/death, mortality, stroke and re-admission following CAS, probably due to CAS data being underpowered. However, the North East was associated with significantly reduced risk of not being discharged home whereas London was associated with increased risk of prolonged LOS following CAS. Whilst these results should be interpreted with caution due to wide CIs, they were adjusted for multiple confounders. Further investigation is required to identify regional differences in selection, referral and management of patients undergoing CEA and CAS that may be contributing to variation in outcomes nationally.

Similar regional variation in procedural outcomes has been reported in other cardiovascular operations. Helder *et al*.[103] reported procedural mortality ranging from 14.5-25.6% following repair of acute Type A Aortic Dissections in 9 regions of the USA between 2004-2016. Significant regional variation in mortality was also reported in the USA following both open and endovascular repair of ruptured AAAs whilst wide variation was identified in LOS and post-operative MI following open and endovascular repair of non-ruptured AAAs.[104] Reasons for regional variation in surgical outcomes may relate to different patient selection criteria for surgery.[104] By standardising practice nationally, this may improve procedural outcomes. Regional differences in procedural outcomes may also be caused by some areas having higher-volume centres than others. More uniform establishment of such centralised 'centres of excellence' across the country may further reduce variation in outcomes.

Trends in Long-Term Outcomes

Our finding that 5-year risk of mortality and stroke was significantly lower following CEA than CAS is in keeping with RCT results.[82-85] However, this remained significant even after the peri-procedural period was excluded, contrary to RCTs[82, 84, 85, 87-90] but supported by Registry studies.[92, 93] This disparity in findings may be explained by case selection whereby more co-morbid patients may undergo CAS than CEA in contemporary practice whilst this selection bias is minimised by randomisation in RCTs. This is why RCTs are more reliable in assessing long-term efficacy of interventions than administrative datasets (which may estimate procedural risks more reliably than RCTs). Differing characteristics of populations analysed in administrative datasets compared to RCTs may also explain why long-term rates of combined procedural stroke/death and ipsilateral stroke were lower in RCTs than our dataset.[82-86, 90, 91]

A further reason for differences in long-term CEA and CAS outcomes between RCTs and administrative datasets may be due to strict credentialing in RCTs. CREST-1[84] only allowed Surgeons to enrol patients following a formal audit of their practice, validated selection process and a minimum volume of 13 CEAs per annum with a complication rate of less than 3% and 5% in asymptomatic and symptomatic patients respectively. Interventionalists were eligible after evaluating their experience, CAS outcomes and participation in a lead-in phase prior to the RCT commencing.[84, 105] Such optimal conditions may produce better results in RCTs than administrative datasets which capture procedures performed by Surgeons and Interventionalists of all experience and proficiency. A final reason for increased risk of post-procedural complications following CAS than CEA may be due to CEA preventing contralateral or vertebrobasilar artery strokes. This was initially described in ICSS.[83] However, our dataset was unable to differentiate between ipsilateral and contralateral strokes, requiring further investigation.

This study has demonstrated overlap between risk factors contributing to adverse procedural and long-term CEA and CAS outcomes. Whilst prior stroke, advanced age, comorbidities and increased deprivation appeared to be associated with adverse procedural and long-term CEA outcomes, non-White ethnicity only affected procedural outcomes. Regarding CAS, prior stroke, advanced age and CHF were associated with adverse procedural and long-term outcomes. Non-White ethnicity was also associated with increased long-term mortality following CAS. Such a detailed analysis of risk factors for procedural and long-term outcomes has never been performed and our result that females are not at increased long-term risk compared to males following CEA or CAS is consistent with other RCTs.[85, 87, 88, 91] Our finding that DM and CRF predict long-term mortality following CEA has also been reported elsewhere.[95] However, RCT findings that older patients derive long-term benefit from CEA compared to CAS[85, 87, 88, 91] is not supported by our data as age 60 years and above was associated with increased long-term stroke risk following both CEA and CAS. This disparity may be explained by more co-morbid patients in our study than RCTs, potentially reducing the benefit of CEA compared to CAS. Our cohort of patients undergoing CEA were also significantly older than those that received CAS. Advanced age may suggest increasing comorbidity, contributing to adverse long-term CEA outcomes in our study compared to RCT findings as this effect would have been minimised by randomisation. Strict credentialing in RCTs may also account for worse CEA outcomes in our study than expected, as previously discussed. Further work should identify and optimise modifiable risk factors for procedural and long-term CEA and CAS outcomes to maximise their effectiveness, potentially making CEA and CAS equivalent in procedural and long-term safety.

Strengths

This is the first report of temporal and regional trends in CEA and CAS procedural outcomes in English HES data. This is also the first report of long-term CEA and CAS outcomes in HES data with identification of risk factors for adverse procedural and long-term outcomes.

Most of this study's strengths are similar to the previous chapter: large sample size (n=68,897) over 16 years; unselected cohort of patients representing English practice; precisely defined cohort due to use of OPCS-4 and ICD-10 codes; and minimal missing data.

Additionally, multivariate logistic regression allowed adjusting of trends for potential confounders, increasing reliability of findings. The use of 3 primary and 3 secondary procedural outcomes also provided a broader, holistic analysis that may be more relevant to patients than traditional endpoints (e.g. stroke/death, mortality and stroke).

Limitations

Most of this retrospective study's limitations are similar to the previous chapter: difficulty in defining symptomatic patients; only including admitted patients; and potential coding inaccuracies. Furthermore, not all confounders may have been identified. Perhaps the biggest limitation is the relatively smaller numbers of patients undergoing CAS, causing some analyses to be underpowered with wide CIs. Lack of ethnic diversity also requires replication in a different setting on a larger scale, including patients from more heterogeneous backgrounds.

Conclusions and Implications

IHD, PVD, DM, CRF, age 70 years and above and non-White ethnicity were associated with significantly increased risk of adverse CEA procedural outcomes. Increased deprivation was associated with significantly increased procedural risk of mortality and prolonged LOS following CEA but did not affect CAS outcomes whilst non-White ethnicity was associated with significantly prolonged LOS following CAS. Prior stroke and CHF were associated with adverse CEA and CAS procedural outcomes whereas female gender was associated with secondary outcomes. There was overlap between risk factors for adverse procedural and long-term CEA and CAS outcomes. Since 2001, procedural stroke/death, mortality and LOS improved whilst re-admission worsened following CEA. Procedural stroke/death, mortality, stroke and LOS did not change over time following CAS but risk of not being discharged home significantly worsened. There was also regional variation in CEA and CAS procedural outcomes. Whilst these findings may improve patient selection for these interventions, further investigation is required to understand reasons for worsening of some CEA and CAS procedural outcomes over time, their regional variation and differences in long-term outcomes post-procedurally.

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CHAPTER 8: Summary and Conclusions

The human and economic burden of stroke is substantial[1] but up to a quarter of thrombo-embolic strokes may be prevented by performing CEA or CAS.[2] However, as demonstrated in this thesis, despite halving long-term stroke risk, carotid interventions involve a substantial risk of harm occurring because the patient pathway is complex and patients themselves are usually co-morbid. According to the literature, iatrogenic harm commonly occurs in healthcare encounters, contributing to considerable morbidity and mortality.[3-14] However, in many cases, adverse events may be preventable, especially in surgical patients.[6-10, 12, 14, 15]

The primary objective of this research project was to identify how the carotid intervention pathway could be improved. This thesis aimed to: identify hospital-level structural factors that affect CEA and CAS procedural outcomes; identify failures in the CEA pathway of symptomatic patients and suggest safeguards to prevent adverse events; identify temporal and regional trends in CEA and CAS provision and procedural outcomes; and identify patient-level risk factors that may affect procedural and long-term CEA and CAS outcomes.

This chapter will summarise findings from this project in the context of research methodologies used before suggesting recommendations. Clinical implications of the most important results will be discussed before limitations and suggestions for future work are presented.

Summary of Findings

A combination of qualitative and quantitative methodologies were used to gain insights into human actions and experiences when examining the CEA pathway whilst allowing objectivity and neutrality when confirming or refuting associations during data analysis.

A systematic review of 17 studies published in the last 15 years (including almost 125,000 patients from 6 countries) identified that structural factors significantly affect CEA and CAS outcomes. Large hospitals, serving large populations, with vascular beds, large SICUs with designated Intensivists, established pathways of care and Vascular Surgeons performing CEA were all associated with better procedural outcomes. Data on CAS were limited.

These findings were used to conduct an ethnographic observational study to identify structural factors that may contribute to causing harm or potential harm in symptomatic patients undergoing CEA. In over 1,000 hours of observations, patient safety incidents were frequent, occurring approximately every 10 hours, with the commonest failures being related to documentation, public health awareness and the environment delivering care. This allowed targeting of these factors to improve quality of care.

An HFMEA was undertaken and recommendations suggested by a multi-disciplinary panel of 13 stakeholders to mitigate against the 65 organisational failures identified. These included improving patient education for identifying stroke symptoms, increasing resources, implementing technology, standardising care and improving communication. These practical suggestions may help optimise the CEA pathway.

Quantitative analyses were then performed in the HES administrative dataset to identify temporal and regional trends in CEA and CAS provision and outcomes and associations between patient-level risk factors and both procedural and long-term CEA and CAS outcomes. A pilot study was first undertaken to understand some of the problems in analysing administrative data. Rates of procedural complications, analysed in the GC dataset (consisting almost 19,000 patients), were found to be broadly consistent with RCT findings but, whilst reflective of contemporary practice, data from administrative datasets may be subject to selection bias and coding issues. These findings were used to inform subsequent analyses.

A 16-year analysis of almost 70,000 English patients undergoing CEA and CAS in the HES dataset found that both CEA and CAS age-standardised rates had reduced since 2011-2012 and there was regional variation in their provision. There was also potential selection bias with older, affluent, White patients being significantly more likely to receive CEA but patients with CHF, IHD and PVD more likely to undergo CAS. This identified factors that may affect CEA and CAS outcomes, requiring further investigation.

The final study reported temporal improvements in most CEA procedural outcomes but regional variation in CEA and CAS outcomes. Factors such as prior stroke and CHF were associated with adverse CEA and CAS procedural outcomes. IHD, PVD, DM, CRF, age 70 years and above and non-White ethnicity were significantly associated with increased risk of adverse CEA procedural outcomes. Increased deprivation was significantly associated with increased risk of procedural death and LOS following CEA but did not affect CAS outcomes whilst non-White ethnicity was associated with significantly prolonged LOS following CAS. There was overlap between risk factors for procedural and long-term adverse CEA and CAS outcomes.

Utilisation of several research methodologies allowed assessment of different aspects of the carotid intervention pathway and identification of areas that could be targeted for optimisation. Evidence-based recommendations arising from the above findings are suggested below that may be implemented to improve the quality of care delivered throughout all aspects of the carotid intervention pathway.

Recommendations

Community Factors

1. Patients should be educated to more effectively identify stroke symptoms
2. GPs, ED Physicians and Opticians should be educated to recognise subtle stroke symptoms
3. GP Practices should open on weekends and Public Holidays
4. GPs should have longer appointments and provide virtual consultations
5. Patients should be made aware of services available at different hospitals

Hospital Factors

1. Stroke and vascular services should be centralised to the same site, where possible
2. Vascular units performing CEA should serve populations greater than 75,000 people
3. Hospitals performing CEA should have 280 beds or more and a vascular ward
4. Parking charges should be abolished in hospitals with more parking spaces made available
5. Hospital transport should be improved

Surgical Factors

1. CEA should preferentially be performed by Vascular Surgeons
2. There should be a 7-day CEA operating list, including on weekends and Public Holidays
3. Patients with prior stroke, CHF, IHD, PVD, DM or CRF need pre-procedural optimisation
4. NBM time should be minimised pre-operatively
5. Consultant of the Week model should be supplemented with a Carotid Consultant

Clinical Factors

1. Delay from symptoms to CEA should be minimised
2. Pathways of care should be established to streamline and standardise care
3. An ICU with 7 or more beds should be in the hospital where CEA is performed
4. There should be a selective admissions policy to SICU following CEA (not routine)
5. There should be a designated Intensivist for the SICU
6. Delivery of patient care should be Consultant-led
7. There should be daily ward rounds, including on weekends and Public Holidays
8. Allied healthcare staff should work on weekends and Public Holidays
9. TIA clinics should run on weekends and Public Holidays with access to CT/MRI scans
10. Infection control practices should be prioritised

Non-Technical Factors

1. There should be increased resource allocation (especially funding for staff recruitment)
2. Technology should be used to improve communication, documentation and prescribing
3. A culture of non-hierarchical, MDT working should be fostered
4. Effective handovers and induction should be implemented
5. Communication should be improved between healthcare staff and patients

Clinical Implications

Many recommendations were suggested by the HFMEA, demonstrating its clinical utility in improving the quality of healthcare delivery. These recommendations are supported by reports from the VSGBI[16] and GIRFT[17] which also suggest centralisation of Vascular Surgery, Consultant-led care, vascular wards, Critical Care facility with Intensivist on-site, minimum population to be served, weekend operating, reduced time from symptoms to CEA, investment in workforce recruitment and establishing protocols to standardise care.[16, 17] Analyses from the UK Government[18], the King's Fund[19] and the CQC[20] have also recommended increasing resources, implementing technology and standardising care, in keeping with this thesis' recommendations. However, this research project has also identified novel areas that may contribute to reducing harm in patients undergoing carotid interventions. For example, minimising NBM time in patients receiving CEA, having a designated on-call Carotid Consultant with their own CEA list, improving induction and handovers, fostering non-hierarchical MDT working, prioritising infection control practices, increasing GP appointment times and educating GPs, ED Physicians, Opticians and patients to recognise subtle stroke symptoms. This thesis' most pertinent recommendations are discussed below.

One of the most important recommendations is to educate patients to improve their ability to recognise stroke symptoms more effectively. In Chapter 3, none of the patients recognised they were having a stroke, TIA or amaurosis fugax and 3 patients had recurrent neurological episodes before contacting medical services. This is a public health failure as up to 40% of recurrent strokes occur within 24 hours of the initial event.[21] In Chapter 4, patients not recognising their stroke symptoms was the highest-scoring failure mode. It is established that the public's stroke knowledge is inadequate[22-24], despite media campaigns such as FAST encouraging patients to present to ED as soon as they experience a neurological event. Stroke

media campaigns have also not caused sustained changes in care-seeking behaviour[25, 26] whilst the few studies examining educational interventions to improve stroke recognition have either been underpowered, unrealistically thorough to implement in clinical practice or unable to show long-term improvements.[27-30] Therefore, patient education should be a public health priority to prevent serious complications from recurrent strokes that may harm patients if they do not recognise their initial event. Sustaining initial improvements in knowledge following education or media campaigns will be the challenge that needs to be effectively overcome.

Another important recommendation is to foster a culture of non-hierarchical, MDT working. Given the current pressures on NHS frontline staff, this suggestion may be difficult to implement. According to a House of Commons Briefing Paper, ED attendances increased by 4.9% in 2019, with 31% of patients waiting more than 4 hours for assessment in December 2019 (target: 5% or less).[31] Over the last decade, ED attendances have increased by 10.6% which is the equivalent of 4,000 extra people attending daily.[31] The number of people waiting for planned treatment has also increased by 44% in the last 5 years (target not met since March 2016) with 73% of NHS Trusts not meeting the 62-day cancer target.[31] A 31% increase in delayed discharges compared to 6 years previously has mostly been caused by delays in organising packages of care in patients' homes prior to discharge and awaiting nursing or care home places.[31] This contributed to half of NHS Trusts having bed occupancy above 90% between July – September 2019, leading to 1.1% of elective surgeries being cancelled on the day whilst the number of surgeries being cancelled twice or more were 16% higher in 2019 than 2018.[31] This unprecedented strain on NHS staff has been further exacerbated by a recent contract dispute with the Government culminating in strikes by Junior Doctors and a pension tax issue that caused Consultants to reduce their hours or retire early, potentially impacting patient care. Low staff morale has contributed to 19% of NHS employees experiencing harassment, bullying or abuse from colleagues and this is higher in healthcare professionals

from black or ethnic minority backgrounds.[32] Incivility has previously been shown to reduce performance by 20-30%[33] whilst 48% of recipients of uncivil behaviour reduce their time at work.[34] Therefore, a non-confrontational environment should be promoted and implemented in healthcare. By taking a system approach to understanding human error, as demonstrated in this thesis, it may be possible to implement a culture of openness to encourage learning from adverse events following CEA and CAS rather than apportioning blame to individuals.[35]

This thesis has also highlighted the potential for technology to transform the delivery of healthcare. Whether this is used to provide virtual consultations for GPs and outpatients or digitalise patient records and prescribe medications electronically, technology could streamline care.[35] Moreover, adverse events could be minimised by prompts to prevent unsafe prescribing whilst algorithms may minimise human error by standardising patient care. Whilst cutting-edge technology is regularly used in operations and interventions, systems in the NHS inhibit the ability to carry out effective patient care. Examples such as difficulties in locating patient notes and faxed referrals not being received were highlighted in Chapters 3 and 4. Implementing technology may enhance the ability of healthcare professionals to perform their jobs safely, effectively and efficiently, potentially improving CEA and CAS outcomes.[35]

Finally, this thesis has shown the potential of administrative data analyses to answer clinical questions. Chapter 5 demonstrated that procedural CEA and CAS outcomes from a large international dataset were comparable to RCT findings but more contemporaneous and generalisable whilst Chapters 6 and 7 highlighted the power of using routinely collected data to examine trends in provision and outcomes both temporally and regionally. It is likely that future research will increasingly harness the power of large administrative datasets to provide contemporary estimates of procedural risk to improve patient care but RCTs will still be required to reliably assess long-term efficacy of interventions.[35]

Limitations

This thesis aimed to identify structural factors that could be optimised to improve CEA and CAS outcomes. Therefore, process factors were excluded. There were also relatively small numbers of CAS patients in all studies, leading to some analyses being underpowered with wide CIs. Volume-outcome analyses were excluded as there is established evidence for this association whilst all primary data analysed were from economically developed countries, limiting generalisability of findings.

The systematic review (Chapter 2) was limited by inclusion of retrospective, heterogeneous studies of varying quality whilst recommendations from the ethnographic study and HFMEA (Chapters 3 and 4) may not be fully generalisable as observations were performed in 3 English hospitals. Some incidents may have also been missed as there was only a single observer.

Quantitative analyses in Chapter 5 were limited by possible selection bias of included patients, self-reporting of procedural complications, the inability to capture events beyond 7 days post-procedure or in settings other than hospital whilst use of proxy measures may have over-estimated procedural strokes in symptomatic patients undergoing CEA. Analyses of HES data in Chapters 6 and 7 were limited by difficulties in reliably defining symptomatic patients, possible coding inaccuracies and inclusion of only inpatients. Not all confounders may have been identified and a lack of ethnic diversity in some analyses are further limitations.

Future Work

Recommendations from this thesis should be implemented and their effectiveness in improving CEA and CAS outcomes audited before potentially being incorporated into national guidelines.

The principal focus of this thesis has been related to CEA. Further investigation is required to identify structural factors that affect CAS outcomes. Identifying novel structural factors (such as MDT working or access to imaging) and their effect on CEA and CAS outcomes should also be researched. More high-quality studies will allow meta-analysis to provide the highest level of evidence on the effect of structural factors on CEA and CAS procedural outcomes.

An observational study and HFMEA of asymptomatic patients undergoing CEA and also symptomatic and asymptomatic patients undergoing CAS should be performed. These studies would need to represent national practice so would require observations in several hospitals and an HFMEA panel from across the UK. Taken together, their results may contribute to constructing an optimal carotid intervention pathway for all patients.

Quantitative analyses have also provided a platform for further research, especially for patients undergoing CAS. Further investigation is required to understand reasons for declining CEA and CAS rates in recent years and regional variation. Reasons for regional variation in CEA and CAS procedural outcomes and worsening of some outcomes over time also require clarification whilst analysis of more CEA and CAS outcomes (e.g. procedural MI) would further inform trends. Future research should also focus on reasons for increased CEA use in affluent, White patients and adverse procedural CEA outcomes in non-White patients from more deprived backgrounds. The effect of degree of affluence/deprivation on CAS procedural outcomes and female gender on CEA and CAS procedural outcomes also requires further clarification. Lack of ethnic diversity requires replication in a different setting on a larger scale,

including patients from more diverse backgrounds, to form more reliable conclusions regarding the effect of ethnicity on CEA and CAS outcomes.

Further clarity is also required regarding worse post-procedural long-term CAS outcomes compared to CEA and to understand why non-White ethnicity is associated with increased long-term mortality following CAS whilst increased deprivation is associated with increased long-term stroke risk following CEA. Increased clarity regarding long-term CEA and CAS outcomes may also be provided by analysing long-term MI risk and subdividing all-cause mortality into constituent parts to further refine patient selection for these procedures to maximise long-term benefit. The effect of age on long-term CEA and CAS outcomes requires further investigation whilst the identification of more modifiable patient-level risk factors for adverse procedural and long-term CEA and CAS outcomes may allow more effective pre-procedural optimisation.

Final Conclusions

This research project has used multiple methodologies to demonstrate that organisational factors can be improved to optimise the carotid intervention pathway. Whilst CEA and CAS provision has reduced in recent years, procedural outcomes have generally improved over time. Modifiable patient characteristics have also been identified that can be targeted to further improve procedural and long-term CEA and CAS outcomes.

By implementing these findings and this thesis' recommendations, it may be possible to optimise the carotid intervention pathway to maximise the effectiveness of CEA and CAS and reduce harm in the vulnerable group of patients undergoing these procedures.

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APPENDICES

APPENDIX I: Data Extraction *pro forma* (Chapter 2)

Authors: **Journal:**

Year of Publication: **Years included in Study:**

Country:

Study Design: RCT/Cohort/Case-controlled/Observational

CEA or CAS:

Surgeon (and Specialty) or Radiologist:

Vascular Surgeon/General Surgeon/Neurosurgeon/Cardiothoracic Surgeon/Radiologist

Number of Centres: **Number of Patients:**

Symptom Status: Symptomatic/Asymptomatic/Both

Does the study report on: Smoking status/Age/Gender/Diabetes status/AF

Structural Factor(s) Investigated:

Vascular Specialist performing intervention/effect of a trainee/dedicated ICU/dedicated intensivist/hospital bed capacity/availability of dedicated vascular beds

Any other relevant factor(s) investigated:

Mortality (%, p): **Combined Death/Stroke (%, p):** **Fatal Stroke (%, p):**

Total Stroke (%, p): **Minor Stroke (%, p):** **Disabling Stroke (%, p):**

MI (%, p):

Length of Stay (Days, p):

Cost ($, p):

Overall Quality (Newcastle-Ottawa Scale for Observational studies or Cochrane Risk of Bias Tool for RCTs):

APPENDIX II: Approvals for Qualitative Studies (Chapters 3 and 4)

Kamran Gaba

From:	JOHNSON, Nigel (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST) <nigel.johnson1@nhs.net>
Sent:	09 April 2019 14:35
To:	Kamran Gaba
Cc:	BULBULIA, Richard (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Subject:	RE: Proposed QIP for carotid patients
Attachments:	RE: Proposed QIP for carotid patients

Dear Kamran,

Thank you for forwarding me your project proposal. Chris Foy has responded to my email confirming that it would be a QI project rather than research as the work concerns one site only, and so is not generalizable.

Therefore, I would advise that you contact our Quality Improvement Manager Alexandra Purcell. Email: alexandra.purcell@nhs.net contact number 0300 422 5756.

I am not sure whether you have had any response from Andrew Seaton but I would certainly chase this with Alexandra.

Kind Regards

Nigel Johnson
Research Portfolio Support Officer& Non-Clinical Staff Governor
Membership Officer of the Diversity Network
Gloucestershire Research Support Service
1st Floor, Leadon House |Gloucester |Gloucestershire | GL1 3NN
Gloucestershire Hospitals NHS Foundation Trust
☎(0300 422) 5467 | nigel.johnson1@nhs.net

If you wish to become a member of the GHNHSFT Diversity Network or have any queries regarding the network, please email us on: ghn-tr.diversitynetwork@nhs.net

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From: Kamran Gaba [mailto:kamran.gaba@ndph.ox.ac.uk]
Sent: 08 April 2019 09:03
To: JOHNSON, Nigel (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Cc: BULBULIA, Richard (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Subject: RE: Proposed QIP for carotid patients

Dear Mr Johnson

Many thanks for considering my proposal to conduct an observational study in Cheltenham.

I have attached the QIP project proposal for your information.

I look forward to hearing the outcome from your discussions.

Best wishes,

Kamran

Kamran Gaba

From: MCLAREN, Gabriella (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST) <gabriella.mclaren@nhs.net>
Sent: 15 April 2019 08:34
To: BULBULIA, Richard (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Cc: Kamran Gaba
Subject: Project registration SG190408

Dear Richard and Kamran,

Thank you for your project registration, it has been approved and given the registration number SG190408.

Please get in touch if there is anything we can do to assist.

Best Wishes,

Gabriella McLaren
Quality Improvement Facilitator
2nd Floor, Flat 42 Robinswood House, Gloucestershire Royal Hospital GL1 3NN
0300 422 5650

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NHS
Gloucestershire Hospitals
NHS Foundation Trust

Vascular Surgery Dept
Mr Richard Bulbulia
Consultant Vascular Surgeon

Summer 2019

TO WHOM IT MAY CONCERN

This letter authorises Kamran Gaba, a visiting DPhil student from the University of Oxford to have right of access to the theatres, wards and ancillary departments at Gloucestershire Hospitals NHS FT between May and August 2019 to follow the patient pathway for carotid surgery and observe how care is delivered in the clinical environment. This will include accessing patient notes and interviewing/discussing aspects of care with healthcare professionals. It will not include any patient care or interference in the clinical management of patients.

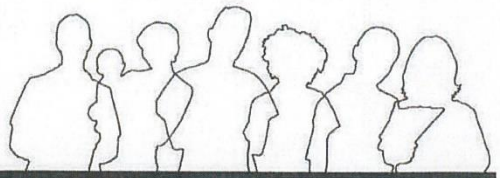
Dates May to August 2019 inclusive

This has been organised by Mr Richard Bulbulia Consultant Vascular Surgeon in conjunction with the University of Oxford.

Yours faithfully

Mr Richard Bulbulia
Consultant Vascular Surgeon

Chair: Peter Lachecki
Chief Executive: Deborah Lee



Great Western Hospitals NHS
NHS Foundation Trust

The Great Western Hospital
Marlborough Road
Swindon
SN3 6BB

Tel: 01793 604020
www.gwh.nhs.uk

4th June 2019

Dear Dr Kamran Gaba

Honorary Appointment as a Clinical Attachment/Observer in Stroke Medicine

I have pleasure in confirming the above Honorary appointment as a Clinical Attachment/Observer at The Great Western Hospital within the Great Western Hospitals NHS Foundation Trust. This post will commence on the 17th June 2019 and will be terminating on the 30th June 2019.

This is an honorary appointment for which no payment will be made by the Trust. This post is subject to the Trust's Policies and Procedures.

This post is for observation only.

May I point out that the Trust does not accept responsibility for the personal property of the staff and you are therefore advised to affect the necessary insurance cover.

I would be grateful if you could kindly confirm in writing, your acceptance of this honorary appointment as soon as possible.

Yours sincerely

Danny Little
Head of Medical Workforce

I confirm that I accept the above honorary appointment.

Print Name: KAMRAN GABA

Signature: ..... Date: 07/06/2019

Our Values
Service Teamwork Ambition Respect

Kamran Gaba

From: PURCELL, Alexandra (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST) <alexandra.purcell@nhs.net>
Sent: 20 August 2019 09:11
To: JOHNSON, Nigel (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST); Kamran Gaba
Subject: RE: Proposed QI project

Dear Kamran (and Nigel),

Thank you for the proposal. Having reviewed it I am happy for the original registration to encompass this part of the project also. The original study was in effect the 'baseline' data collection with this section moving into the diagnostics of what can be done to improve safety and how this can be achieved.

Best wishes,
Alex

Alexandra Purcell
Quality Improvement Manager
☎ x5756

From: JOHNSON, Nigel (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Sent: 19 August 2019 11:17
To: Kamran Gaba
Cc: PURCELL, Alexandra (GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST)
Subject: RE: Proposed QI project

Dear Kamran,

Thank you for this. Could I please advise that you speak to Alexandra Purcell in the first instance as she works in the QI team and is best placed to advise you.

From an R&D perspective we could then provide local trust approval.

Kind Regards
Nigel

Nigel Johnson
Research Portfolio Support Officer& Non-Clinical Staff Governor
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APPENDIX III: Participant Information Sheet (Chapter 3)

Participant Information Sheet: Ethnographic Observational Study

Introduction

You are being invited to take part in a quality study, aiming to improve the care of patients who have had a stroke or 'mini-stroke'. Before you decide whether you wish to participate, it is important to understand why this study is being done and what it will involve. Please read the following information carefully and discuss with others (family, friends, etc.) if you wish.

Why have I been chosen?

You have been invited to take part in this study because you are receiving care in hospital following a stroke or 'mini-stroke'. The study team will observe what happens to you during your treatment. We hope to better understand how services work together to prevent certain types of strokes.

Do I have to take part?

No – taking part is entirely voluntary. Should you decide to take part, you can change your mind at any time without giving a reason and it will make no difference to the care you receive.

What will happen to me if I take part?

A member of the study team will observe all aspects of your hospital stay. We will be focusing our attention on the doctors, nurses and other healthcare professionals who are involved in your care and the health records which they create. During the period of observation, the observer will not be involved in your care.

The study will also include a review of your health records after your discharge from hospital.

What are the possible benefits and negatives to me?

We cannot promise the study will help you directly but the information we collect may help to improve care for other patients in the future. This an observational study so there is no risk to participants. However, if you have any concerns, you can raise them with the study team.

Will my taking part in this study be kept confidential?

All information that is collected about you during the study will be kept strictly confidential. During the study, we need to be able to identify you, using your NHS number or hospital reference number (MRN), to match records created at different times. By consenting to take part in the study you are also consenting to us accessing your health records and using your identifiable data for this purpose.

Once the observation period is completed, information which may identify you will be removed from the study's records. Nobody will then be able to identify you from those records.

You may withdraw your consent to participate in the study at any time by contacting the study lead at **kamran.gaba@ndph.ox.ac.uk** or by phoning **07960 739 163**. In the event that you withdraw your consent to participate in the study, all information relating to you will be deleted.

During the time we hold identifiable personal data, the University of Oxford and Gloucestershire Hospitals NHS Foundation Trust act as joint data controllers. You can find more information about privacy and your rights as a patient at https://www.gloshospitals.nhs.uk/privacy-notice/

Our findings may be discussed with other researchers but that will only be on the basis of our anonymised records.

What will happen to the results of the study?

The results collected in this study will be analysed and findings will be published in scientific journals to improve the quality of care for future patients. This will also use only aggregated and anonymised data and you will not be identifiable from any published material.

Who is organising and funding the study?

The University of Oxford, in conjunction with Gloucestershire Hospitals NHS Foundation Trust, is organising this study, which is funded by the Medical Research Council and the Nuffield Department of Population Health (University of Oxford).

Who has reviewed the study?

This study has been approved by the Nuffield Department of Population Health (University of Oxford) and the Gloucestershire Research Support Service (Gloucestershire Hospitals NHS Foundation Trust). Approval from Clinicians has also been actively sought and provided.

Thank you very much for agreeing to participate in this study

APPENDIX IV: Pre-Hospital Questionnaire (Chapter 3)

Defining the Carotid Intervention pathway in a United Kingdom Hospital: an ethnographic observational study

Pre-Hospital Questionnaire

1. What symptoms did you experience?
2. When did you experience them?
3. Have you experienced this before?
4. When did you seek medical advice?
5. Did the GP explain what happened?
6. Did the GP prescribe medications?
7. When were you referred to the Stroke team?
8. How did you get to the hospital?
9. When did you arrive at the hospital?
10. Did you have some blood tests taken?
11. Have they requested a scan yet?
12. What did the scan show?
13. Have they prescribed your tablets?
14. Have your questions been answered?
15. Are you satisfied with your care?
16. Any other comments

APPENDIX V: Ethnographic Observations *pro forma* (Chapter 3)

Patient MRN: **DoB/Age:** **Gender:** **Comorbidities:** **Tel:**

Clinical Assessment(s)	Investigations	Management	Communication	Documentation	Prescribing	Timing	Environment	Staffing/MDT participation	Infection Control

APPENDIX VI: Staff Questionnaire (Chapter 3)

Staff Questionnaire

1. Can you talk me through the pathway that a stroke patient requiring carotid intervention at your unit undergoes from initial presentation until discharge post-procedure?

2. What is the population size that your unit serves?
   How many beds are in your hospital? How many beds do you have for Vascular patients?

3. Tell me about access to CT scanners, interventional radiology and emergency theatre in your unit, both in hours and out of hours?

4. Do you have defined pathways of care for patients undergoing carotid intervention? If so, please describe them

5. Who decides when to operate/intervene? Is there MDT involvement?

6. Are patients pre-assessed prior to carotid intervention? If so, how?

7. Who performs the intervention (Consultant/Trainee/non-Vascular Specialty)?

8. Who reviews the patients post-procedurally? When is a Consultant review undertaken?

9. How large is your ICU? Is it only for surgical patients?
   Is there a dedicated Intensivist? How willing are they to review and/or accept CEA patients?

10. Any other comments?

APPENDIX VII: HFMEA Scoring Matrix (Chapter 4)

Score	Frequency	Severity	Detectability
4	High (1 per day)	Death	Remote
3	Moderate (1 per week)	Any Disability	Low
2	Infrequent (1 per month)	Increased Length of Stay	Moderate
1	Very Infrequent (1 per year)	Nil Effect	High

Overall Pathway

Number	Process Step	Failure Mode(s)	Effect	Mean F	Mean S	Mean D	Mean F x S x D
1	Patient experiences symptoms	Patient does not recognise symptoms as stroke	Delay in seeking medical assistance	2.75	3.38	2.13	**19.72**
2	Patient contacts GP Practice	GP does not return patient's call/GP Practice closed (weekend/Public Holiday)	Delay in clinical assessment	2.13	2.63	1.88	**10.46**
3	GP reviews patient	GP does not recognise symptoms as stroke	No referral made to TIA clinic	1.75	2.50	1.75	**7.66**

4	Optician reviews patient	Optician does not recognise symptoms as amaurosis fugax	No referral made to TIA clinic	1.75	2.50	2.25	**9.84**
5	Patient/family member/friend calls Ambulance	Patient/family member/friend does not call Ambulance	Delay in clinical assessment	2.38	3.13	2.50	**18.55**
6	Patient/family member/friend drives to ED	Patient/family member/friend drives to a hospital that does not have a HASU	Patient requires transfer to a different hospital for assessment by Stroke team	2.25	2.63	2.00	**11.81**
7	Patient triaged in ED	Patient not triaged in ED	Delay in being assessed by ED Doctor	2.25	2.38	2.25	**12.02**
8	Patient reviewed by ED Doctor	Stroke not diagnosed	Delay in being assessed by Stroke Consultant	1.88	2.75	2.00	**10.31**
9	CT brain imaging performed in ED	CT brain imaging not performed in ED	Delay in stroke diagnosis	2.50	2.75	2.00	**13.75**
10	Patient referred to Stroke team (inpatient)	Patient not referred to Stroke team	Delay in being assessed by Stroke Consultant	2.25	2.88	1.63	**10.51**
11	Patient transferred to HASU (inpatient)	Patient not transferred to HASU	Potential for mismanagement	1.88	3.38	2.25	**14.24**
12	TIA clinic referral made (outpatient)	Referral does not arrive/arrives over weekend or Public Holiday	Delay in being assessed by Stroke Consultant	2.38	2.75	2.13	**13.88**
END OF 'DIAGNOSTIC' PATHWAY							

13	TIA clinic referral triaged by Stroke Consultant	Stroke Consultant fails to recognise urgency of referral	Delay in being assessed by Stroke Consultant	1.13	3.00	2.00	**6.75**
14	TIA Clinic Coordinator calls patient to schedule appointment	Patient does not answer their telephone/has a commitment on the suggested date	Delay in being assessed by Stroke Consultant	2.50	3.13	2.13	**16.60**
15	Patient attends TIA clinic (outpatient)	Patient does not attend TIA clinic appointment	Delay in being assessed by Stroke Consultant	1.88	3.13	2.25	**13.18**
16	Stroke Consultant reviews patient	Stroke not diagnosed	Delay in clinical management	1.50	2.88	1.88	**8.09**
17	Stroke Consultant orders Carotid Dopplers (+/- CT brain imaging)	No space for imaging requests or delay over weekend/Public Holiday	Delay in clinical management	1.88	3.29	1.88	**11.55**
18	Stroke Consultant reviews results of imaging/medical notes	Stroke Consultant does not review imaging/medical notes not available	Potential for mismanagement	1.75	3.13	2.13	**11.62**
19	Stroke Consultant alters patient's medications	Stroke Consultant does not alter patient's medications	Potential for recurrent stroke	2.00	2.71	2.25	**12.21**
20	Stroke Consultant refers patient to Vascular Surgery via e-referral	Referral does not arrive/arrives out-of-hours	Delay in being assessed by Vascular Consultant	1.88	2.88	2.13	**11.46**
21	Stroke Consultant discusses referral with Vascular Consultant	Stroke Consultant does not discuss referral with Vascular Consultant	Potential delay in being assessed by Vascular Consultant	1.38	2.88	2.00	**7.91**
END OF 'STROKE MEDICINE' PATHWAY							

22	Vascular Coordinator discusses referral with Vascular Consultant	Vascular Consultant fails to recognise urgency of referral	Delay in being assessed by Vascular Consultant	1.17	3.50	2.17	**8.85**
23	Vascular Coordinator calls patient to schedule vascular review	Patient does not answer their telephone/has a commitment on the suggested date	Delay in being assessed by Vascular Consultant	1.83	2.83	2.33	**12.12**
24	Patient attends review with Vascular Consultant (CGH)	Patient does not attend review with Vascular Consultant	Delay in being assessed by Vascular Consultant	1.67	2.83	2.17	**10.23**
25	Vascular Consultant reviews patient on GRH HASU (inpatient)	Vascular Consultant does not review patient on GRH HASU	Patient requires transfer to CGH or attends vascular ward (CGH) for review	1.50	2.50	2.00	**7.50**
26	Patient transferred to vascular ward (CGH)	Patient not transferred to vascular ward (CGH) – e.g. no beds	Delay in clinical management	1.67	3.17	2.17	**11.44**
27	Vascular Consultant reviews results of imaging/medical notes	Vascular Consultant does not review results of imaging/medical notes not available	Potential for mismanagement	1.40	3.60	1.80	**9.07**
28	Vascular Consultant advises CEA	Patient unsure about whether to proceed – family discussion	Delay in clinical management	2.40	3.60	1.60	**13.82**
29	Vascular Consultant suggests MDT discussion	Vascular Consultant does not suggest MDT discussion	Potential for inappropriate CEA or delay in CEA (resulting in recurrent symptoms)	1.60	2.20	1.40	**4.93**

30	Pre-operative assessment scheduled as outpatient (CGH)	Patient unable to attend pre-operative assessment on suggested date	Delay in clinical management	2.00	2.20	2.00	**8.80**
31	Pre-operative assessment scheduled as inpatient (CGH)	Pre-operative assessment unable to be performed/not thoroughly performed	Delay in clinical management/post-CEA complication	1.60	2.00	1.80	**5.76**
32	CEA scheduled (CGH) via telephone	Cancelled/delayed on day of surgery/miscommunication regarding CEA date/delay over weekend or Public Holiday	Delay in clinical management	2.00	2.60	1.60	**8.32**
33	Repeat Carotid Doppler pre-operatively	No repeat Carotid Doppler pre-operatively	Potential for mismanagement	1.60	2.60	1.60	**6.66**
34	Vascular Consultant review pre-operatively	No Vascular Consultant review pre-operatively	Potential for mismanagement	1.20	2.40	1.60	**4.61**
35	Pre-operative checks (including consent)	No pre-operative checks/not consented by Vascular Consultant	Potential for mismanagement	1.40	2.80	1.60	**6.27**
36	Transferred to Operating Theatre	Not transferred to Operating Theatre	Delay in clinical management	1.25	2.50	1.20	**3.75**
37	WHO checklist in Operating Theatre	No WHO checklist in Operating Theatre	Potential for mismanagement	1.00	2.00	1.40	**2.80**
38	CEA performed by Vascular Consultant	CEA not performed by Vascular Consultant	Potential for mismanagement	1.40	2.20	1.60	**4.93**

39	Admitted to Recovery post-CEA	Not admitted to Recovery	Post-operative complications may not be detected	1.20	2.80	1.60	**5.38**
40	Admitted to HDU post-CEA for hypotension	Not admitted to HDU	Post-operative hypotension may not be treated	1.60	3.00	1.40	**6.72**
41	Transferred to vascular ward post-CEA	Not transferred to vascular ward post-CEA	Inappropriate environment for post-operative management (e.g. noisy)	1.40	2.80	1.80	**7.06**
42	Daily Vascular Consultant-led ward round	No daily Vascular Consultant-led ward round	Clinical management being suggested by junior team members – potential for mismanagement	1.20	2.20	2.00	**5.28**
43	Ward round entry clearly and accurately documented	Ward round entry not clearly and accurately documented	Potential for miscommunication and mismanagement	1.20	2.00	2.00	**4.80**
44	Post-operative instructions followed	Post-operative instructions not followed/not documented	Potential for mismanagement	1.60	3.00	2.00	**9.60**
45	Referral to other medical specialties for advice/management	No referral to other medical specialties	Potential for mismanagement	1.60	2.60	1.60	**6.66**
46	Medications prescribed correctly post-CEA	Medications prescribed incorrectly post-CEA	Potential for the patient to have an adverse event	1.60	3.00	1.60	**7.68**
47	Decision to eat/drink	No decision to eat/drink	Prolonged NBM time period	1.20	1.60	1.20	**2.30**

48	Infection control practices appropriate	Omissions in hand washing	Potential for spread of infections	1.60	2.60	1.80	**7.49**
49	Staffing levels appropriate (including Vascular Consultants)	Multiple Vascular Consultants involved in the care of a single patient	Potential for omissions in clinical assessment and management	2.00	2.00	1.40	**5.60**
50	Efficient discharge	Inefficient discharge	Delay in leaving hospital	1.80	2.20	2.00	**7.92**
51	Plan for outpatient review	No plan for outpatient review	Potential for post-CEA complications to not be detected and/or treated	2.00	2.67	1.67	**8.89**
END OF 'VASCULAR SURGERY' PATHWAY							

Abbreviations – CEA: Carotid Endarterectomy; CGH: Cheltenham General Hospital; CT: Computerised Tomography; D: Detectability; ED: Emergency Department; F: Frequency; GP: General Practitioner; GRH: Gloucestershire Royal Hospital; HASU: Hyper-Acute Stroke Unit; HDU: High Dependency Unit; MDT: Multi-Disciplinary Team; NBM: Nil By Mouth; S: Severity; TIA: Transient Ischaemic Attack; WHO: World Health Organisation.

APPENDIX VIII: Publications, Presentations and Awards

Work conducted during this research project has contributed to the publications listed below.

Book Chapter

Gaba KA & Halliday A. Epidemiology and Indications for Revascularization of Carotid Stenoses. In: Faggioli G, Halliday A, Pini R, Gallitto E, Stella A. Carotid Disease: Clinical and Morphological Insights. Turin: Edizioni Minerva Medica S.p.A.; 2017.

Peer-Reviewed Publications

Gaba KA, Morris DR, Halliday A, Bulbulia R, Chana P. Improving Quality of Carotid Interventions: Identifying Hospital-Level Structural Factors that can Improve Outcomes. *Ann Vasc Surg* 2020. [Article Accepted for Publication – in Press]

Gaba KA, Halliday A, Bulbulia R, Chana P. Procedural Risks of Carotid Intervention in 19,000 patients. *Ann Vasc Surg* 2021; 70: 326-331.

Gaba KA, Vincent C, Chana P. Learning Lessons from the Coronavirus-induced Disease 2019 Pandemic to Improve Outcomes Following Carotid Interventions. *Ann Vasc Med Res* 2020; 7 (4): 1116.

Gaba KA & Bulbulia R. Identifying Asymptomatic Patients at High-Risk for Stroke. *J Cardiovasc Surg (Torino)* 2019; 60 (3): 332-344.

Gaba KA, Ringleb PA, Halliday A. Asymptomatic Carotid Stenosis: Intervention or Best Medical Therapy? *Curr Neurol Neurosci Rep* 2018; 18 (11): 80.

The ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. *N Engl J Med* 2018; 379 (16): 1529-1539.

The ASCEND Study Collaborative Group. Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus. *N Engl J Med* 2018; 379 (16): 1540-1550.

Abstract Publications

Gaba KA, Chana P, Morris DR, Landray M, Bulbulia R, Halliday A. Improving the Quality of Carotid Endarterectomy and Carotid Artery Stenting: Identifying Hospital-Level Structural Factors that Affect Outcomes in the Prevention of Thromboembolic Strokes. *Eur J Vasc Endovasc Surg* 2019; 58 (6): e347-348.

Poorthuis M, Morris DR, **Gaba KA**, Howard DPJ, de Borst GJ, Bulbulia R, Halliday A. The UKCCS Collaborative Group. Contemporary Stroke Risks of Patients with Asymptomatic Carotid Stenosis: Design and Characteristics of a Large Prospective Cohort Study. *Eur J Vasc Endovasc Surg* 2019; 58 (6): e854.

Gaba KA, Chana P, Landray M, Halliday A, Bulbulia R. Risk of Death and Stroke in 19,000 Patients Undergoing Carotid Endarterectomy or Stenting: an Analysis of the Dr Foster Global Comparators' Dataset. *Eur Stroke J* 2018; 3 (1S): 44-45.

International Oral Presentations

Gaba KA, Chana P, Morris DR, Landray M, Bulbulia R, Halliday A. Improving the Quality of Carotid Endarterectomy and Carotid Artery Stenting: Identifying Hospital-Level Structural Factors that Affect Outcomes in the Prevention of Thromboembolic Strokes.

European Society for Vascular Surgery (ESVS) 32nd Annual Meeting, Valencia (Spain), September 2018

Gaba KA, Chana P, Landray M, Halliday A, Bulbulia R. Risk of Death and Stroke in 19,000 Patients Undergoing Carotid Endarterectomy or Stenting: an Analysis of the Dr Foster Global Comparators' Dataset.

4th European Stroke Organisation Conference (ESOC), Gothenburg (Sweden), May 2018

International Poster Presentations

Poorthuis M, Morris DR, **Gaba KA**, Howard DPJ, de Borst GJ, Bulbulia R, Halliday A. The UKCCS Collaborative Group. Contemporary Stroke Risks of Patients Undergoing Duplex of the Carotid Arteries: Design and Characteristics of a Large Prospective Cohort Study.

9th Munich Vascular Conference 2019, Munich (Germany), December 2019

Morris DR, Poorthuis M, **Gaba KA**, Howard DPJ, de Borst GJ, Bulbulia R, Halliday A. The UKCCS Collaborative Group. Contemporary Stroke Risks of Patients with Asymptomatic Carotid Stenosis: Design and Characteristics of a Large Prospective Cohort Study.

European Society for Vascular Surgery (ESVS) 33rd Annual Meeting, Hamburg (Germany), September 2019

Several additional abstracts will be submitted to international conferences.

Awards

December 2019	UKCCS Collaborative Group awarded 'Best Poster' at the 9th Munich Vascular Conference (MAC)
September 2019	UKCCS Collaborative Group awarded 'Best e-Poster Presentation' at the European Society for Vascular Surgery (ESVS) 33rd Annual Meeting, Hamburg (Germany)
December 2018	Awarded a Participation Grant to attend the 8th Munich Vascular Conference (MAC)
October 2017	Awarded a Medical Sciences Graduate School Scholarship at the University of Oxford to study for a DPhil in Population Health (jointly funded by the Medical Research Council and Nuffield Department of Population Health)