WHAT ARE THE OPTIMAL TREATMENT STRATEGIES IN PEOPLE OF INCREASED STROKE RISK DUE TO CAROTID STENOSIS: USING CLINICAL TRIAL AND EXTERNAL DATA TO EVALUATE LONG-TERM BENEFITS AND COST-EFFECTIVENESS?

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APPENDICES FOR

THESIS SUBMITTED FOR THE DEGREE OF

Doctor of Philosophy

MICHAELMAS 2018

Table of Contents

List of Appendix Text

List of Appendix Tables

List of Appendix Figures

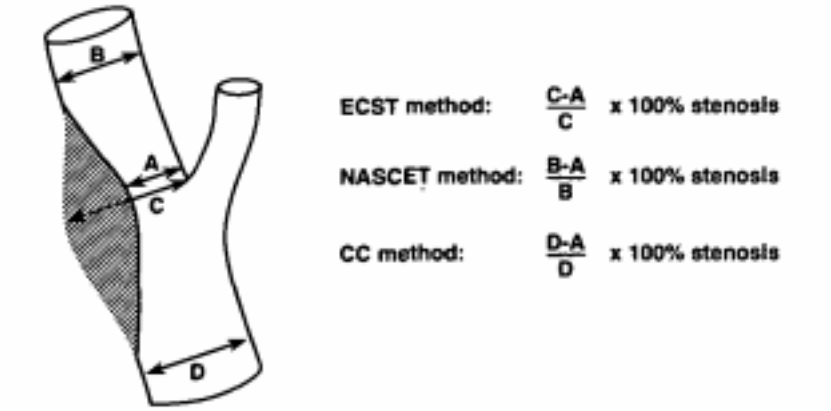
Appendix material for Chapter 1

Introduction

Appendix Text 1.1: Methods of measurement of degree of stenosis

There are two main methods commonly used to measure the degree of stenosis in the carotid artery, the distal artery diameter narrowing (North American Symptomatic Carotid Endarterectomy Trial (NASCET)) method, and the local (diseased) diameter narrowing (European Carotid Surgery Trial (ECST)) method.(1) In both methods the lumen diameter is measured at the point of maximum stenosis, but the denominator in the equation used to calculate the degree of stenosis is different. In ECST the estimated normal lumen diameter at the site of the lesion is used, based on a visual impression of where the normal arterial wall was before development of the stenosis, while in NASCET the diameter of a visible portion of disease-free Internal Carotid Artery (ICA) distal to the stenosis is used (**figure 1.1**). A third method uses the diameter of the visible disease-free distal common carotid artery (**figure 1.1**).(2)

Figure 1.1: Measuring degree of stenosis



**Sourced from Rothwell P. et al (1994) (2)*

Appendix Text 1.2: Conventional carotid endarterectomy (CEA) technique

When using the conventional CEA technique, where a longitudinal incision is made in the carotid artery, the incision is closed either using a primary closure technique (where the incision is sutured together) or using patch angioplasty where the patch is made out or synthetic material or the patient's own vein. The use of patch angioplasty may help reduce the risk of the carotid artery narrowing during suture placement. However, thin-walled vein patches carry the possibility of rupturing and possible fatal outcomes, while synthetic patches may result in infections.(3) Evidence from a systematic review that includes 10 Randomised Control Trials (RCTs) comparing primary closure with routine patch closure shows that patch closure reduces the combined risk of perioperative and long-term risk of stroke.(4)

Appendix Text 1.3: Eversion CEA technique

An alternative to the conventional CEA technique is eversion CEA, where an oblique division of the ICA is performed at its origin, the plaque removed through means of eversion (i.e. turning the internal carotid artery inside out to remove the plaque), and the ICA re-implanted. In a review published in 2001 including 5 trials, it was concluded that there was no significant difference between eversion and conventional CEA with regard to procedural and long-term risks.(5) An analysis of 563 patients who were randomised to the CEA arm of the SPACE trial[1], shows that while eversion CEA had a significantly higher rate of ipsilateral stroke or death within 30 days, the 2 year risk of ipsilateral stroke occurring after 30 days is significantly greater in the conventional CEA group.(6)

[1] Stent-Protected Angioplasty Versus Carotid Endarterectomy trial; Recruitment period: 2001-2006

Appendix Text 1.4: Shunting during CEA procedure

Shunting during the endarterectomy procedure is either done routinely, selectively, or not employed at all, dependent on the surgeon's preference. In selective shunting, if under general anaesthesia, the need for shunting maybe determined by either electroencephalographic monitoring, measuring carotid stump back pressure, somatosensory evoked potential monitoring or transcranial Doppler monitoring.(7) When CEA is performed under local anaesthesia, the surgeon and anaesthetist monitors awake the patient when determining the need for shunting, with common indicators used including the patient being unable to move the contralateral limb, or being unresponsive to questioning, before employing a shunt.(8) , Results from a RCT comparing routine versus selective shunting shows that while perioperative strokes were lower for routine shunting when compared to selective shunting (0% vs 2%), the differences are not statistically significant (p=0.498).(9)

Appendix Text 1.5: Types of stents used in carotid artery stenting (CAS) procedure

Types of stents historically used in the CAS procedure include (i) open cell stents which have larger free cell areas between the metallic struts of the stent thus offering more flexibility, (ii) closed cell stents which have a denser metallic mesh with smaller free cell areas thus providing more effective plaque coverage, and (iii) hybrid stents which have properties of both open and closed cell stent designs, with newer versions entering the market consistently. Although open cell stents seem more likely to allow plaque pieces to break off and embolize distally casing strokes, a study carried out across 10 European centres show that while stroke/death risks within 30 days of procedure was higher when using closed cell design stents when compared to open cell design stents (3.1% vs 2.4%), the differences were not statistically significant (p=0.38).(10)

Appendix Text 1.6: Use of protection devices during CAS procedure

During the CAS procedure, the manipulation of plaque by the use of catheters, wires, balloons and stents may release embolic particles, thus causing blockages in the smaller arteries leading to the brain and leading to neurological deficits. This may be avoided by the placing of a protection device above the area in which the stent is placed. There are three types of protection devices commonly used: filters, distal occlusion balloons and proximal occlusion balloons. A review using data from the global carotid artery stent registry shows that patients in whom protection devices were used have a lower rate of stroke or procedural death when compared to those where no device was used (2.23% vs 5.29%; $p<0.0001$).(11)

Appendix material for Chapter 2

A systematic review and critical appraisal of cost-effectiveness studies comparing treatment methods for carotid stenosis

Appendix Table 2.1: CHEERS checklist for reporting economic evaluations of health interventions

Section/Item	Item No	Patel S. (1999)	Cronen-wett J. (1997)	Henrik-sson M. (2008)	Thapar A. (2013)	Young K. (2010)	Almekhlafi M. (2014)	Kilaru M. (2003)	Morris S. (2016)	Mahoney E. (2011)	Khan A. (2012)	Maud A. (2010)	Vilain K. (2012)	Janssen M. (2008)	Luebke T. (2013)	Sum across all studies
Title and abstract																
Title – identifies as economic evaluation	1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Abstract - objectives, perspective, setting, methods, results and conclusion	2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Introduction																
Background and objectives – study question and relevance to health policy	3	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Reporting of Methods																
Target population and subgroups	4	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	I	Y	13.5
Setting and location	5	N	N	Y	Y	N	N	N	Y	N	N	N	Y	Y	N	5

Section/Item	Item No	Patel S. (1999)	Cronen-wett J. (1997)	Henrik-sson M. (2008)	Thapar A. (2013)	Young K. (2010)	Almekhlafi M. (2014)	Kilaru M. (2003)	Morris S. (2016)	Mahoney E. (2011)	Khan A. (2012)	Maud A. (2010)	Vilain K. (2012)	Janssen M. (2008)	Luebke T. (2013)	Sum across all studies
Study perspective	6	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Comparators – which interventions are compared	7	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Time horizon of study	8	N	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	10
Discount rate	9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	13
Choice of health outcomes used as measures	10	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Measurement of effectiveness: Describes fully the design features (if from single study) or methods of identification (if from synthesis based estimates)	11	P	P	I	I	Y	Y	Y	Y	Y	Y	Y	Y	I	N	10.5
Population and methods used to elicit preference for outcomes	12	N	P	Y	I	N	Y	I	Y	Y	Y	I	Y	I	N	8.5

Section/Item	Item No	Patel S. (1999)	Cronen-wett J. (1997)	Henrik-sson M. (2008)	Thapar A. (2013)	Young K. (2010)	Almekhlafi M. (2014)	Kilaru M. (2003)	Morris S. (2016)	Mahoney E. (2011)	Khan A. (2012)	Maud A. (2010)	Vilain K. (2012)	Janssen M. (2008)	Luebke T. (2013)	Sum across all studies
Estimating resources and cost: Describe fully methods used to estimate resource use (if single study based) or approaches and data sources (if model based study)	13	Y	P	Y	I	I	Y	Y	Y	Y	Y	I	Y	Y	N	11
Currency, price date, and conversion	14	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	R	14
Clear description of choice of model of evaluation	15	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	R	14
Describes all assumptions made in model	16	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	R	14
Describes all analytic methods used in evaluation	17	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	R	12
Results																
Reports values, ranges, references,	18	Y	P	Y	I	Y	I	I	Y	I	N	Y	Y	Y	R	10.5

Section/Item	Item No	Patel S. (1999)	Cronen-wett J. (1997)	Henrik-sson M. (2008)	Thapar A. (2013)	Young K. (2010)	Almekhlafi M. (2014)	Kilaru M. (2003)	Morris S. (2016)	Mahoney E. (2011)	Khan A. (2012)	Maud A. (2010)	Vilain K. (2012)	Janssen M. (2008)	Luebke T. (2013)	Sum across all studies
and if used, probability distributions of all parameters																
Reports incremental costs and outcomes	19	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	R	13
Characterizing uncertainty of incremental results	20	P	P	Y	Y	Y	Y	I	Y	Y	I	Y	Y	Y	R	11
Reports differences in parameters when characterizing heterogeneity	21	Y	Y	Y	Y	N/A	N/A	N	Y	Y	Y	N/A	Y	N/A	N/A	8
Discussion																
Study findings, limitations, generalizability, and current knowledge	22	N	Y	Y	Y	I	Y	I	Y	Y	Y	Y	Y	Y	R	12
Other items of reporting																

Section/Item	Item No	Patel S. (1999)	Cronen-wett J. (1997)	Henrik-sson M. (2008)	Thapar A. (2013)	Young K. (2010)	Almekhlafi M. (2014)	Kilaru M. (2003)	Morris S. (2016)	Mahoney E. (2011)	Khan A. (2012)	Maud A. (2010)	Vilain K. (2012)	Janssen M. (2008)	Luebke T. (2013)	Sum across all studies
Source of funding	23	N	N	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	N	9
Conflicts of interest	24	N	N	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	N	8
TOTAL		15.5	15.5	22.5	22	20	21.5	17.5	24	22.5	20.5	19	24	19.5	17	

Y – Reported (score:1) ; N – Not reported (score: 0); P – Partially reported (score: 0.5); N/A – not applicable since heterogeneity not characterised

Appendix Table 2.2: Information on procedural and long-term stroke risks used in economic evaluations

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Henriksson M. (2008)(12)	30 day risks	SWEDVASC	CEAs performed in Sweden (1994 – 2003); Mean age: 70	Men: No Event (0.983), Disabling stroke (0.005), Non-disabling stroke (0.007), Death (0.005) Women: No Event (0.962), Disabling stroke (0.017), Non-disabling stroke(0.017), Death (0.004)	
	Long-term annual stroke risks: MT patients	MT arm of ACST-1 trial (limited to Swedish patients)	ACST-1 trial (1993 – 2003); Mean age: 72	Men: 2.81%; Women: 1.68%	
	Relative Risk from CEA vs MT (only to 5 years) for non-perioperative stroke	ACST-1		0.345	
	Outcomes of non-procedural stroke	ACST-1 (limited to Swedish patients)		Fatal stroke (0.241); Disabling stroke (0.276); Non-disabling stroke (0.483)	
	Mortality not related to stroke	SWEDVASC	Using Weibull time-to-event proportional hazards model (Variables: Age)		
Patel S. (1999)(13)	CEA 30 day risks	NASCET	Mean age: 66 Results from patients with 50% to 69% stenosis	Source: NASCET (only ipsilateral) CEA: Death (0.012), Minor Stroke (0.046), Major Stroke (0.008) MT: Death (0.004), Minor Stroke (0.01), Major Stroke (0.01)	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Long-term annual stroke risks: MT patients	NASCET		Year 1: Minor Stroke (0.067), Major Stroke (0.026) Year 2: Minor Stroke (0.029), Major Stroke (0.011) Year 3 onwards: Minor Stroke (0.021), Major Stroke (0.009)	
	Long-term per annum stroke risks: CEA patients	NASCET		Year 1: Minor Stroke (0.024), Major Stroke (0.006) Year 2 onwards: Minor Stroke (0.016), Major Stroke (0.004)	:
	Proportion of fatalities in major strokes	ECST and NASCET		0.18	
	Excess mortality of major stroke survivors	Baum H. et al (1981)(14)	National Stroke survey: 1971-76	0.077	
	Excess mortality of symptomatic patients	Norris J. et al (1991)(15)	696 asymptomatic patients referred to Doppler laboratory and followed for mean time of 41 months. Study period not reported/	0.063	
	Age specific annual mortality	US life tables	Year 1988		
Cronenwett J. (1997)(16)	CEA 30 day risks	ACAS		Stroke/Death (0.023)	
	Long-term annual stroke risks	ACAS		CEA: Ipsilateral Stroke (0.006), Recurrent Stenosis (0.006), Major	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
				Stroke (0.013) MT: Ipsilateral Stroke (0.0023)	
	Long-term annual absolute risks of CEA after MT due to TIA or Minor Stroke	NASCET		0.0058	
	Proportions of major strokes in ipsilateral strokes	ACAS (source stated in discussion)		0.5	
	Proportion of fatal strokes in major strokes	Based on 2 population based studies Sacco R. et al (1991) and Bonita R. et al (1993)	Sacco R. et al (1982):5209 subject aged 30 to 62 in 1949 from Framingham, Massachusetts followed for 26 years Bonita R. et al (1993): Stroke events registered in Auckland, New Zealand in 1981 and 1991 – Auckland stroke study	0.15	:
	Recurrent stenosis needing re-operative CEA			0.6%	
	Excess mortality	ACAS	Non-stroke mortality rate in whole ACAS population	0.5%	Added to age and sex specific mortality rates in the UK (year or source not stated).

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Thapar A. (2013)(17)	CEA 30 day risks	ACST-1	ACST-1 trial (1993 – 2003); Mean age: 72	Stroke/Death (0.029)	Unclear: How non-perioperative strokes were split to fatal, disabling and non-disabling. Assumed it was split using ACST-1 information.
	Non-procedural annual stroke risks	ACST-1		Annual Stroke/Death: CEA – 0-5 years: 0.009; 0-10 years: 0.014 MT - 0-5 years: 0.021; 0-10 years: 0.016	
	Non-stroke related mortality	UK Life tables 2007-09	By deducting stroke related mortality from all-cause mortality.	Age and gender specific – number not reported.	
	Increase in mortality following stroke	Oxford Community Stroke Project(18)	675 patients, followed up to 6.5 years. Study period not given	Multiple not reported	Consisted with findings in Perth, Australia.
Young K. (2010)(19)	30 day risks	Meta-analysis (ITT population) of Kentucky, SAPPHIRE, SPACE, EVA-3S		CEA: Death (0.0126), Minor Stroke (0.0266), Major Stroke (0.0202), MI (0.0131) CAS: Death (0.0062), Minor Stroke (0.0381), Major Stroke (0.0321), MI (0.0064)	
	Long-term annual absolute risks:	Weighted average of 2-year SPACE, 3-year SAPPHIRE, and 4-year EVA-3S results		CEA: Annual Excess Death (0.0096), Annual Stroke (0.0210) CAS: Annual Excess Death (0.015), Annual Stroke (0.04)	
	Proportion major strokes in long-term strokes:	Not reported		0.3	:

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Proportion of fatal strokes in Major strokes	Not reported		0.139	
Almekhlafi M. (2014)(20)	CEA 30 day risks	Published Meta-analysis of 12 RCTs*(21)	Full text not available	CEA: Death (0.009), Minor Stroke (0.022), Major Stroke (0.006), MI (0.018)	*Published study did not report outcomes by major/minor stroke. Thus data were re-analysed to get major/ minor stroke results
	30 day CEA vs CAS relative risks (ORs)	Published Meta-analysis of 12 RCTs*		Death (1.11), Minor Stroke (1.91), Major Stroke (1.645), MI (0.47)	
	Post-procedural annual risks	Outcomes from RCTs which reported long-term results (of 12 RCTs above), deducting 30 day events		CEA: Death (0.018), Minor Stroke (0.0515), Major Stroke (0.013)	:
	Post-procedural CEA vs CAS relative risks (ORs):	Outcomes from RCTs which reported long-term results (of 12 RCTs above), deducting 30 day events		Death (1.02), Minor Stroke (1.3), Major Stroke (1.1)	
Kilaru M. (2003)(22)	CEA 30 day risks	New York Presbyterian Hospital	447 CEAs performed from 1997 - 2001	Major Stroke (0.45%), Minor Stroke (0.45%), Death (0%), Hematomas (2.68%), Restenosis (1%), CNI (1.78%)	
	CAS 30 day risks	Averaged across 4 non-randomised studies		Major Stroke (1.8%), Minor Stroke (3.2%), Death (1.2%), Hematomas (0.8%), Restenosis (3%), CNI (0%)	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
		where study period ranged from 1993-99			
	Post-procedural risks	Not reported			:
	Non-stroke related mortality	Not reported			
Morris S. (2016)(23)	1 year stroke	ICSS	Mean age: 70; Recruitment period: 2001: 2008	CEA: 5.1%; CAS: 9.5%	Obtained from HTA report(24)
	5 years (cumulative) stroke			CEA: 9.4%; CAS: 15.2%	
Mahoney E. (2011)(25)	Stroke	1 year cumulative SAPPHIRE results	Mean age: 73; Recruitment period: 2000-02	Major stroke: CEA: 4%; CAS: 0.6% Minor stroke: CEA: 3.3%; CAS: 5%	
	Death			CEA: 12.6%; CAS: 6.9%	
	MI			CEA: 7.9%; CAS: 2.5%	:
Khan A. (2012)(26)	Strokes (4-year cumulative)	Annual results from CREST 4-year follow-up	Mean age: 69; Recruitment period: 2000-08	CAS: 0.108; CEA: 0.086	
	Death (4-year cumulative)			CAS: 0.113; CEA: 0.126	
	MI			CAS: 0.011; CEA: 0.023	:

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Luebke T. (2016)(27)	Procedural disabling stroke/death	Literature review – unclear as to which source was used	Not reported	CEA: 0.0142	
	Post-procedural annual disabling stroke/death	Literature review – unclear as to which source was used	Not reported	CEA: 0.004 MT: 0.012	
Maud A. (2010)(28)	Stroke	SAPPHIRE at 1 year follow-up	Mean age: 73; Recruitment period: 2000-02	Major strokes: CAS: 0.01; CEA: 0.04 Minor strokes: CAS: 0.04; CEA: 0.02	
	Death			Death: CAS: 0.07; CEA: 0.13	
	MI			MI: CAS: 0.02; CEA: 0.05	:
Vilain K. (2012)(29)	Stroke	CREST at 1 year follow-up	Mean age: 69; Recruitment period: 2000-08	Major strokes: CAS: 0.016; CEA: 0.015 Minor strokes: CAS: 0.014; CEA: 0.006	
	Death			CAS: 0.1; CEA: 0.07	
	MI			CAS: 0.03; CEA: 0.05	:
Janssen M. (2008)(30)	Technical failure during CAS	Global CAS registry(11) – 29 centres across Europe, North and South America and Asia – 12,392 procedures from 1997 to 2002.		1.11%	Peri-operative/ procedural risks not given.

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Post-operative annual major stroke	ECST(31)	Mean age: 63; Recruitment period: 1981-94	0.43%	
	Post-operative annual minor stroke			0.66%	:
	Annual MI			1.59%	
	Death hazard ratio after stroke			2.07	
	Death hazard ratio after disabling stroke			6.05	
	Death hazard ratio after MI			2.09	
	Death hazard ratio after MI and stroke			3.09	
	Prob. of death 6 months after peri-operative dis. stroke			9.30%	
	Prob. of death after dis. stroke			30.8%	
	Prob of death after MI			22.6%	

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; SWEDVASC: Swedish Vascular registry; MI: Myocardial Infarction; Prob: Probability

Appendix Table 2.3: Information on QoL measures used in economic evaluations

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Henriksson M. (2008)(12)	Mean utility of general population	Burstom K. (2001) et al	Cross sectional postal Stockholm County public health survey (n = 4950, 20-88 years) in 1998, using EQ-5D	Assumed less than 1; exact value not stated	Working backwards from Disabling stroke QoL decrement, it can be assumed to be 0.7
	Disabling stroke:	Unclear	Unclear	-0.35	Mean utility of patients with disabling stroke = 0.5. With utility of carotid stenosis population < gen. population, this corresponded to a decrement = 0.35
	Non-disabling stroke	Haacke C. et al (2006) Duncan P. et al (2000)	77 patients admitted to the Department of Neurology, Philipps-University Marburg after stroke or TIA. QoL measured using German version of EuroQoL index (EQ-5D) and Health Utility Index 2 and 3 459 individuals enrolled in a prospective cohort study were assessed within 14 days post stroke and re-evaluated at 1, 3, and 6 months in SF-36 scale	No decrement	
Patel S. (1999)(13)	No event	Not reported	Not reported	Not reported	
	Minor Stroke:	Solomon N. et al (1994)(32)	Full text not available 117 of 209 patients at risk of stroke participated. Patients presented written case scenarios of stroke outcomes and asked to rate between 1 to 100.	QALY = 40% of LY	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Major Stroke	Unclear	Unclear	-0.25	
Cronenwett J. (1997)(16)	No event	Not reported			
	First major stroke	Gage B. et al (1995)	Cost-effective study of warfarin and aspirin, where QoL was obtained by interviewing 74 patients with atrial fibrillation, and time trade-off method used to elicit utilities for 3 types of neurological deficits.	-0.39	No other characteristics of data source population are stated.
	Recurrent stroke			-0.12	
Thapar A. (2013)(17)	Same as Henrikkson et al				
Young K. (2010)(19)	No event	Unclear			Stated QoL for well and death was 1.0 and 0.
	Major stroke	Unclear		0.15	
	Minor stroke	Post P. (2001) et al(33)	A systematic review of utility of health states after stroke. Not stated clearly which source from sys. Review was used.	0.65	
	30 day MI	Unclear		0.88	
Almekhlafi M. (2014)(20)	No event				
	Major stroke	Tengs & Linn meta-analysis(34)	Full test not availbale Sys. Review and meta-analysis for QoL estimates for stroke	0.28	
	Minor stroke	Beaver Dam study)	5,925 participants aged 43-84 in 1987, and were asked of prior medical conditions and the SF-36.	0.64	
	30 day MI	SAPPHIRE	QoL of patients having experienced a MI, after 12 months in SAPPHIRE as reported in Mahoney et al.	0.74	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Kilaru M. (2003)(22)	No event	Not reported			
	Major stroke	Solomon N. et al (1994)(32)	117 of 209 patients at risk of stroke participated. Patients presented written case scenarios of stroke outcomes and asked to rate between 1 to 100.	0.4 times	
	Minor stroke	Unclear		0.25 times	
	30 day MI	Tsevat J. et al (1993)(35)	Time tradeoff scores on 67 MI survivors	0.88 times	
	CNI			-0.15	
	CAS			- 2 days	
	CEA			- 2 weeks	
Morris S. (2016)(23)	Baseline	ICSS		CEA: 0.758 CAS: 0.775	Utility at 3 months, 6 months, and annually until 5 years afterwards was measured using EQ-5D-3L tool in patients in ICSS study to get mean QALYs of each treatment arm
Mahoney E. (2011)(25)	1 year	EQ-5D utility weights measured at 2, 4 weeks, 6 and 12 months in SAPPHIRE.		Not reported	
	Post 1 year No event	Beaver Dam Health Outcomes Study	5,925 participants aged 43-84 in 1987, and were asked of prior medical conditions and the SF-36.	Males: 0.841; Females: 0.833	
	Post 1 year major stroke	Tengs & Linn meta-analysis(34)	Full text not available Sys. Review and meta-analysis for QoL estimates for stroke	0.52	
	Post 1 year minor stroke			0.87	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Post 1 year MI	Tsevat J. et al (1993)(35)	Time tradeoff scores on 67 MI survivors	0.88	
Khan A. (2012)(26)	No event	Reference not clear		0.815	
	Disability stroke			0.718	
	Minor stroke			Not reported	
	30 day MI			0.744	
Luebke T. (2016)(27)	No event	Unclear		1	
	Disabling stroke	Unclear		0.5 for corresponding year and then 0	
Maud A. (2010)(28)	No event	Not reported		0.815	All values are same as Khan et al25)
	Disability stroke	Not reported		0.718	
	Minor stroke	Not reported		Not reported	
	30 day MI			0.744	
Vilain K. (2012)(29)	CEA	CREST		0.704	
	CAS			0.708	
	Major stroke			-0.1 at 1 month; -0.06 at 12 months	Obtained from performing a linear regression from CREST data
	Minor stroke			-0.02 at 1 month; -0.03 at 12 months	
	MI			0	
	CNI			0	
Janssen M. (2008)(30)	Minor stroke	*Tsevat et al (1993)(35)*		0.15	
	Major stroke			0.65	
	MI	*Post et al (2001)(33)*		0.88	:

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; SWEDVASC: Swedish Vascular registry; MI: Myocardial Infarction; QALY: Quality Adjusted Life Year; CNI: Cranial nerve injury

Appendix Table 2.4: Data on costs of treatment methods and cost of stroke in economic evaluations

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
Henriksson M. (2008)(12)	CEA	Resource use for CEA in county of Östergötland, Sweden	As per those reported on Feb 2007. Nothing mentioned about professional fee	6674 Euros	
	MT	Not reported		276 Euros	Includes a doctor's visit and costs of pharmaceutical treatment
	Non-disabling Stroke	Ghatnekar O. (2004) et al	Cost of 213 first strokes in 100,000 Swedish individuals. Includes inpatients care, social services costs, outpatient visits, rehabilitation, drugs, & production losses	First year: Euros 25,263; Subsequent years: Euros 10,526	Only abstract available, thus no information on follow-up and year of study. Costs not given by stroke severity, but proportion of disabling strokes given, which were used in calculation.
	Disabling Major Stroke			First year: Euros 11,579; Subsequent years: Euros 2,105	
Patel S. (1999)(13)	CEA	Cost of CEA procedure: New York Presbyterian Hospital–Cornell Campus Professional fee: Medicare reimbursement for the Current Procedural Terminology code for CEA	Year of costs not given	US$6420	Cost of CEA procedure: US$5,100 Professional fee: US$1,320
	MT	Not reported		US$63 per year	Cost of aspirin therapy
	Minor Stroke	Oster G. (1994) et al(36)	Sourced from cost-effectiveness study using ticlopidine in preventing stroke in high risk patients. Full text of paper not	First year: US$9,300; Subsequent years: US$798	
	Major Stroke			First year: US$51,150; Subsequent years: US$26,880	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
			available and thus information on how these cost were calculated are not available.		
Cronenwett J. (1997)(16)	CEA	Medicare resource based relative value system (RBRVS)	Year of costs not given. Nothing mentioned about professional fee.	US$8,500	Year not stated
	Radiologist cost	Medicare RBRVS		US$1,600	
	Fatal Stroke	Medicare RBRVS		US$6,800	
	Minor stroke	Averaged across 2 published sources	Thorngren M. et al (1991): 258 patients hospitalized 1986-87 in Swedish hosptial and followed for 12 months. Includes hospital care, non-hospital primary care and community care. Terente A. et al (1994): Full text not available. Gives direct cost (from 2 population based studies and 2 nationwide cross-sectional inventories) and indirect costs of stroke care in Sweden in 1991.	US$9,000 (first year cost being 3 times higher as per results from Thorngen et al)	
	Major stroke	Averaged across 3 population based studies.	1 population based study in Thorngen M et al and 2 population based studies in Terente A et al.	US$34,000 for first year; US$18,000 afterwards	
Thapar A. (2013)(17)	CEA	HRG tariffs 2010-11	HRG gives the average unit cost for a specific HRG	£3,345	
	Disabling stroke	First Year: Wardlaw et al (2006)(37)		First year: £29,312 Subsequent years: £14,846	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Non-disabling stroke	Subs year: Sandercock et al	Obtained from sources published in two HTA cost-effectiveness reports	First year: £4,938 Subsequent years: £1,152	
	Community, social services and informal care after disabling stroke:	Patel A. (2004) et al(38)	300 stroke patients in the UK. Client service receipt inventory used to obtain resource use after discharge.	£3,500	
Young K. (2010)(19)	CEA				Assumed to be the same
	CAS				
	Hospitalization costs	Unclear		MI: US$9,100 Minor Stroke: US$9,800 Major Stroke: US$10,500	
	Continuing costs	Unclear		Minor Stroke: US$7500 MI: US$4500 Major stroke (first year): US$66,500 Major Stroke (second year): US$33,900	
Almekhlafi M. (2014)(20)	CEA	Calgary cohort	Cohort of patients who underwent carotid intervention in Calgary, Canada from 2005-07. Includes all direct procedure related costs in-hospital and human resource costs (nurses, therapists and social workers). Physician claims for CEA, CAS and anesthesia were obtained from the Alberta Ministry of Health schedule of medical benefits	CDN$ 2,243	
	CAS			CDN$ 7,303	
	Major/ minor stroke	BURST study	1-year prospective study of ischemic stroke patients recruited at 12 Canadian stroke	Major stroke (first year): CDN$ 83,164 Major Stroke (second year): CDN$ 31,267	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
			centres. Includes emergency services, hospitalizations, rehabilitation, physician services, diagnostics, medications, allied health professional services, homecare, medical/assistive devices, changes to residence and paid caregivers, and indirect costs	Minor stroke (first year): CDN$ 31,136 Minor Stroke (second year): CDN$ 13,488	
	MI	Calgary cohort	See above	MI (first year): CDN$ 4,937 MI (second year): CDN$ 1,455	
Kilaru M. (2003)(22)	CEA	Cost of resources: New York Presbyterian Hospital (year not given), this was multiplied by the resource utilisation in same source. Professional fee: Medicare reimbursement 2002		US$7,871	
	CAS	Cost of resources: New York Presbyterian Hospital (year not given), this was multiplied by the resource utilisation in Literature Professional fee: Medicare reimbursement 2002		US$ 10,133	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Major/ minor stroke	Unclear		Major stroke (first year): US$52,019 Major Stroke (second year): US$27,336 Minor stroke: US$9,419	
	MI	Dangas G. (2001) et al(39) and Yadav J.(1996) et al(40)	Sourced from information from 2 studies. Not clear how exactly.	MI (first year): US$11,000 MI (second year): US$2,800	
Morris S. (2016)(23)	CEA CAS	Resource use data from ICSS and unit costs from published sources. Costs include professional fees			
	Major Stroke Minor Stroke	Cost of managing stroke obtained by using OxVasc data to predict hospital care cost for each patient based on individual risk factors such as age, sex, previous medical history, etc	Patients followed up to 5 years. Hospital records from the Oxford Radcliffe Hospitals NHS Trust were reviewed for any accident & emergency (A&E) visit, emergency transport, outpatient care visit, day case or hospitalisation in OxVASC		
Mahoney E. (2011)(25)	CEA	Using resource use data from SAPPHIRE multiplied by unit costs (taken as avg in 3 study hospitals). Includes personnel costs.		Not reported	
	CAS			Not reported	
	Major/ minor stroke	Based on hospital billing data		Not reported	
	MI			Not reported	
Khan A. (2012)(26)	CEA	National Inpatient Sample based on hospital inpatient data utilization in year 2008.		US$9,335	
	CAS			US$14,972	
	MI			CEA: US$31,289 CAS: US$30,810	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Stroke	Stroke cost stated as taken from National Inpatient Sample based on hospital inpatient data utilization in year 2008. Disabling stroke follow-up cost taken from ACAS study publication(41)		US$45,980	
	Death	Obtained from a previously published cost-effectiveness study(42) – study states that the value they used (US$5,000) was an estimate with no sources listed		US$7,176	
Luebke T. (2016)(27)	CEA	Literature reviews – unclear as to what the exact source is		€4483	
	First year post disabling stroke			€83,164	
	Subsequent years post disabling stroke			€31,267	
	First 30 days post stroke			€6,930	
Maud A. (2010)(28)	CEA	Healthcare Cost and Utilization Project (HCUP) data - National Inpatient Sample Not stated if prof. fees are included		US$11,200	
	CAS			US$6,802	
	Disability caused by major stroke	*Gage et al(42)*		US$10,400	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
	Disability caused by minor stroke		Represents annual direct health system cost of continuing cost after initial hospitalization	US$2,808	
	MI	Healthcare Cost and Utilization Project (HCUP) data		US$8,404	
Vilain K. (2012)(29)	CEA	Resource use was recorded for each procedure in CREST. Costs calculated as the product of resource use and unit cost for each component.	Not sure if professional fees are included	US$6,794	
	CAS			US$5,769	
	Major/ minor stroke	Cost of each patient's post-procedural hospital care calculated using hospital billing data.			
	MI				
Janssen M. (2008)	CEA	Resource use and costs in University Medical Center Utrecht and St Antonius Hospital. Included professional costs. Year not given		€4,012	
	CAS			€5,500	
	Major/ minor stroke	Cost of hospital stay based on Dutch literature Follow-up based on published data	Hospital stay: 2 sources given, but n information on which was used. 5 sources given – not stated as to how they were used. However it is stated that rehabilitation, nursing home	Acute major stroke: 25,769 Major stroke follow-up (1st 6 months): 18,781 Major stroke follow-up (after 6 months): 8,017 Major stroke on death: 7,779 Minor stroke follow-up (1st 6 months): 5,556	

Study	Parameter	Data source	Data source characteristics	Parameter values	Other notes
			and physical therapy costs were given	Minor stroke on death: 4,146 *All costs in Euros	
	MI	Unclear		€15,000	

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; SWEDVASC: Swedish Vascular registry; MI: Myocardial Infarction;

Appendix Table 2.5: Cost-effectiveness results in economic evaluations

Study	Cost-effectiveness results		
	Outcomes	**Characterising uncertainty**	**Characterising heterogeneity**
Patel S. (1999)(13)	Comparison: CEA vs MT Inc Cost: US$580 Inc Benefit: 0.13 QALYs ICER: US$4,462	No PSA performed Deterministic Sensitivity analysis: Procedural risks Post-procedural risks Cost of intervention (US$5,000 to US$15,000) Major stroke costs (US$0 to US$30,000); Minor stroke cost (US$0 to US$5,000); Disutility post major stroke (0.2 to 1.0)	By age: CEA not cost-effective for age > 83 years at a threshold of US$60,000. ICER for 90 year-old patients reported as US$136,740 Only mortality rates adjusted by age.
Cronenwett J. (1997)(16)	Comparison: CEA vs MT Cost: CEA: US$14,448; MT: US$12,407; Inc: US$2,041 Benefits (QALYs): CEA: 8.12; MT: 7.87; Inc: 0.25 ICER: US$8,004	No PSA performed Deterministic Sensitivity analysis: Procedural risks Post-procedural stroke risks All costs discount rate QoL after major stroke	By age: Patients < 71 years old, ICER < US$20,000. At age=79, ICER > US$100,000
Henriksson M. (2008)(12)	Comparison: CEA vs MT (Currency: Euros) Men =65: Cost: CEA: 18.733; MT: 13,898; Inc: 4,835 Benefit: CEA: 8.477; MT: 8.338; Inc: 0.14 ICER: 34,557 Men =75: Inc Cost: 5,381; Inc Benefit: 0.091 QALYs; ICER: 58,930 Women =65: Inc Cost: 7,434; Inc Benefit: 0.024; ICER: 311,133 Women =75: Inc Cost: 7,334; Inc Benefit: 0.009; ICER: 779,776	PSA Performed: Prob of CEA being cost-effective at Euros 52,500 was 70% and 40% for 65-and 75-year old men. For women it was <10% for both 65 and 75-year olds. Deterministic sensitivity analysis: Treatment effect extended to 10, 15 and lifetime of patient Use of standard mortality from life tables instead of estimated mortality Allowing for recurrent stroke	By age and gender Results shown in outcomes Mortality rates and post-procedural stroke risks adjusted by age and gender.
Thapar A. (2013)(17)	Comparison: CEA vs MT	PSA Performed: Inc Cost: £ 942 (95% CI: -73, 1936)	By age and gender (GBP/ QALYs) Men <75 years old: Inc Cost: £360; Inc Ben: 0.085; ICER:

Study	Cost-effectiveness results		
	Outcomes	**Characterising uncertainty**	**Characterising heterogeneity**
	Cost : CEA: £8,496; MT: £7,855; Inc: 641 Benefits (QALYs): CEA: 9.627; MT: 9.537; Inc: 0.09 ICER = £7584	Inc Ben: 0.081 QALYs (95% CI:-0.004; 0.16) Deterministic sensitivity analysis: Using a mean hazard ratio calculated over 10 years Assuming that the rates of stroke in the two arms were the same after 5 years A higher mortality rate post stroke Increased hospital costs of surgery	£3254 Women<75 years old: Inc Cost: £-746; Inc Ben: 0.174 Men>75 years old: Inc Cost: £1894; Inc Ben: 0.026; ICER: 71,699 Women>75 years old: Inc Cost: £2574; Inc Ben: -0.065 Only reported that mortality rates were adjusted by age and gender
Young K. (2010)(19)	CEA: Cost: US$35,200 Benefit: 9.64 QALYs CAS: Cost: US$52,900 Benefit: 8.97 QALYs	PSA performed: Showed CEA was cost-effective at a probability of around 59% at all ranges of willingness to pay. Deterministic sensitivity analysis: Procedural risks Post-procedural stroke risks	Not performed
Almekhlafi M. (2014)(20)	Comparison: CAS vs CEA Cost: CAS: CDN$30,731; CEA: US$24,624; Inc: CDN$6107 Benefit (QALYs): CAS: 6.71; CEA: 6.83; Inc:-0.12	PSA performed: 10,000 Monte Carlo simulations, almost all of which showed CAS had higher costs. CAS: CDN$28,615 (95% CI, $28,556– $28,674); CEA: CDN$22,948 (95% CI, $22,919–$22,976). Results of PSA for benefits not reported Deterministic sensitivity analysis: Discount rate Procedural risl Post-procedural risk Cost of MI Cost of CAS Annual mortality risk	Not performed
Kilaru M. (2003)(22)	CEA: Cost: US$28,772 Benefit: 8.36 QALYs	No PSA performed Deterministic sensitivity analysis:	By age: Reports "CEA remains cost saving even in patients up to 90 years of age. the Cost effectiveness of CEA was

Study	Cost-effectiveness results		
	Outcomes	**Characterising uncertainty**	**Characterising heterogeneity**
	CAS: Cost: US$35,789 Benefit: 8.20 QALYs	Varying procedural risks and cost of procedure	further enhanced in patients who were less than 70 years of age. It was not reported how heterogeneity by age was adjusted for in the Markov model
Morris S. (2016)(23)	Comparison: CAS vs CEA Inc Cost: US$736 (-353, 1826) Inc Benefit: -0.010 (-0.117, 0.097) QALYs	PSA performed iNMB = US$991 ($4,475 to $2494) at US$29,000 maximum willingness to pay per QALY and US$1,118 ($6,110 to $3,875) at US$43,000 Probability of CAS being cost-effective was less than 0.4% for thresholds US$0 to US$50,000	By Age and Gender: Men: Inc Cost: US$481; Inc QALY: -0.055 Women: Inc Cost: US$1123; Inc QALY: 0.103 <70: Inc Cost: US$204; Inc QALY: 0.057 >70: Inc Cost: US$1,112; Inc QALYs: -0.061
Mahoney E. (2011)(25)	Comparison: CAS vs CEA Cost: CAS: $60,528; CEA: $57,187; Inc Cost: US$3,342 Inc QALYs: 0.51 ICER: US$6,555	PSA performed: As willingnyess to pay per QALY of US$50,000, CAS had a 98.3% probability of being cost-effective. Deterministic sensitivity analysis: Using alternative assumptions regarding cost, life expectancy, utility weights, the prognostic impact of non-fatal events, and discount rate	Symp: Inc Cost: US$6,990; Inc Ben: 0.03 QALYs; ICER = US$204,229 Asymp: Inc Cost: US$1,902; Inc Ben: 0.71 QALYs; ICER: US$2,667 Assumptions and data sources for long-term cost and life-expectancy projections was reported by gender, but no cost-effectiveness results.
Khan A. (2012)(26)	Comparison: CAS vs CEA Cost: CAS: $18,335; CEA: 13,276 Average per person QALY CAS: 0.712; CEA: 0.702 ICER = $229,429	PSA performed: At willingness to pay per QALY of $68,000, $100,000, $300,000, and $500,000 per QALY, the probability of CAS being cost-effective was 0.11%, 1.3%, 27.86%, and 44.35%, respectively	Not performed
Luebke T. (2016)(27)	Comparison: CAS vs CEA Inc Cost: €2,946.49 Inc QALYs: 0.03 ICER: €90,230.12	PSA performed: At a willingness to pay per QALY of Euros 50,000, CEA had a 71.8% probability of being cost-effective	Not performed

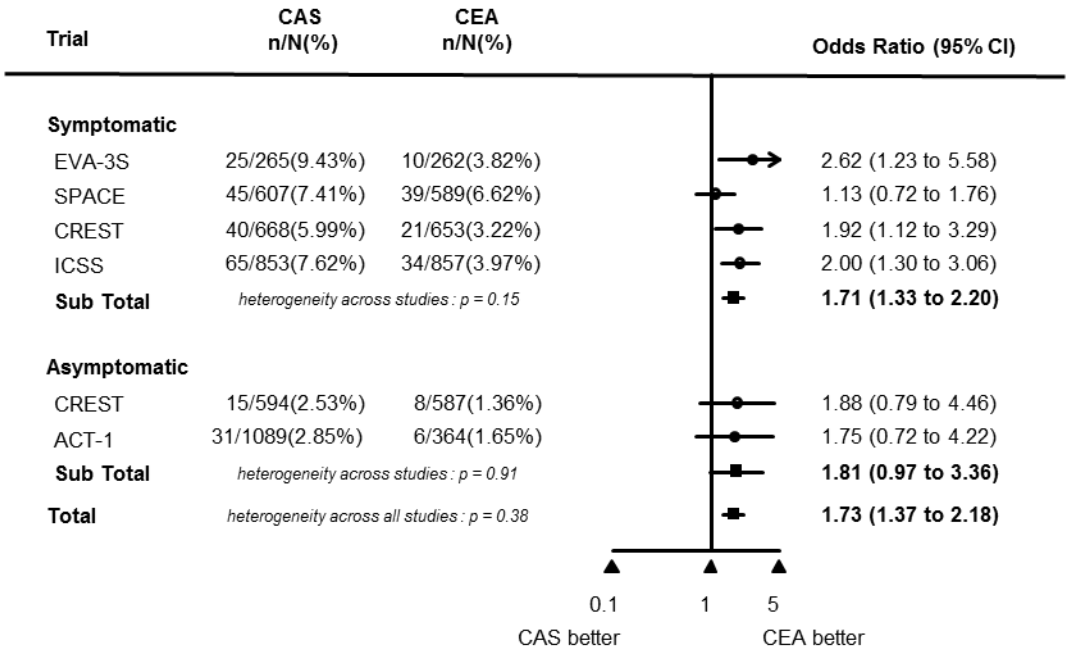
Study	Cost-effectiveness results		
	Outcomes	**Characterising uncertainty**	**Characterising heterogeneity**
Maud A. (2010)(28)	Comparison: CAS vs CEA Cost: CAS: US$12,782; CEA: US$8,916 QALY: CAS: 0.753; CEA: 0.701 ICER : US$67,891 (-$129,372, $379,661)	PSA performed with CIs reported At a willingness to pay of $67,891, CAS had a probability of <40% of being cost-effective	Not performed
Vilain K. (2012)(29)	Comparison: CAS vs CEA Cost: CAS: US$80,141; CEA: US$79,617 QALY: CAS: 4.841; CEA:4.849 ICER: CEA dominant	PSA performed CEA had a 54.4% probability of being cost-effective at a willingness to pay of $50,000	Asymptomatic Cost: CAS: US$80,314; CEA: US$79,705 QALY: CAS: 4.862; CEA:4.859 ICER (CAS vs CEA): US$277,249 Symptomatic: Cost: CAS: US$79,988; CEA: US$79,540 QALY: CAS: 4.823; CEA: 4.840 ICER (CAS vs CEA): CEA dominant
Janssen M. (2008)(30)	Scenario 1 (ECST and Global CAS registry) shows CAS preferred (differences in cost and QALYs not statistically significant) Scenario 2 (Cochrane review) shows CEA preferred (differences in cost and QALYs statistically significant). Incremental results not presented - only in graphical form	PSA performed with CIs in cost-effectiveness plane shown graphically	Not performed

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; SWEDVASC: Swedish Vascular registry; MI: Myocardial Infarction; PSA: Probability Sensitivity Analysis; Inc; Incremental; Sym; Symptomatic; Asymp: Asymptomatic; QALY: Quality Adjusted Life Year; ICER: Incremental Cost-effectiveness ratio

Appendix material for Chapter 3

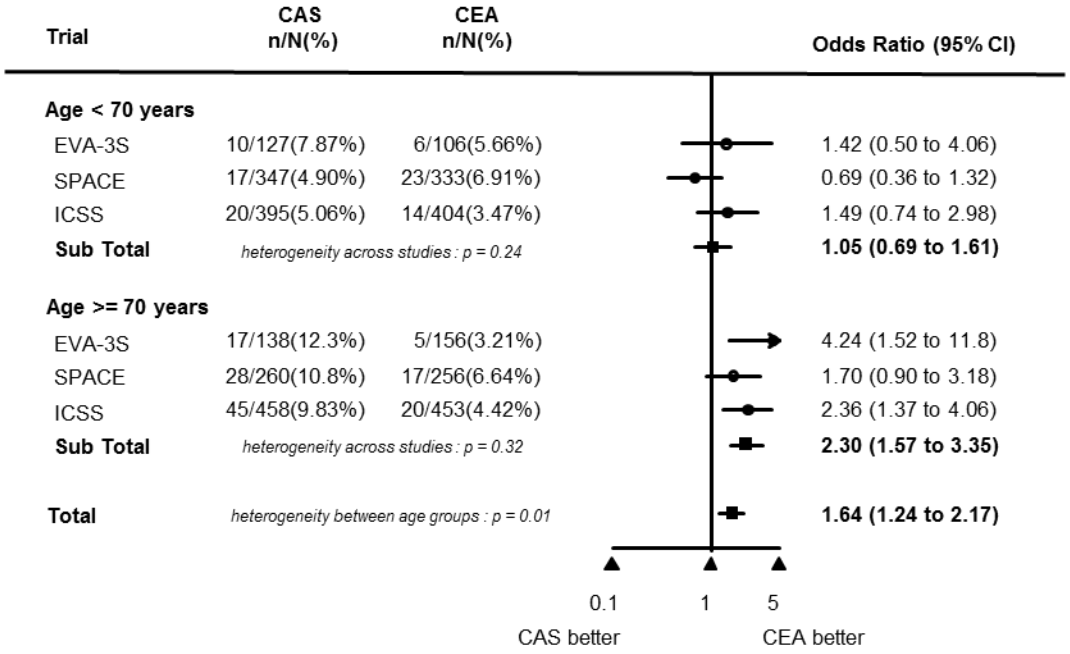
Systematic review and meta-analysis of randomized evidence of procedural, post-procedural and overall effects of CEA and CAS

Appendix Figure 3.1: PROCEDURAL STROKE OR DEATH risks in RCTs comparing CAS vs CEA



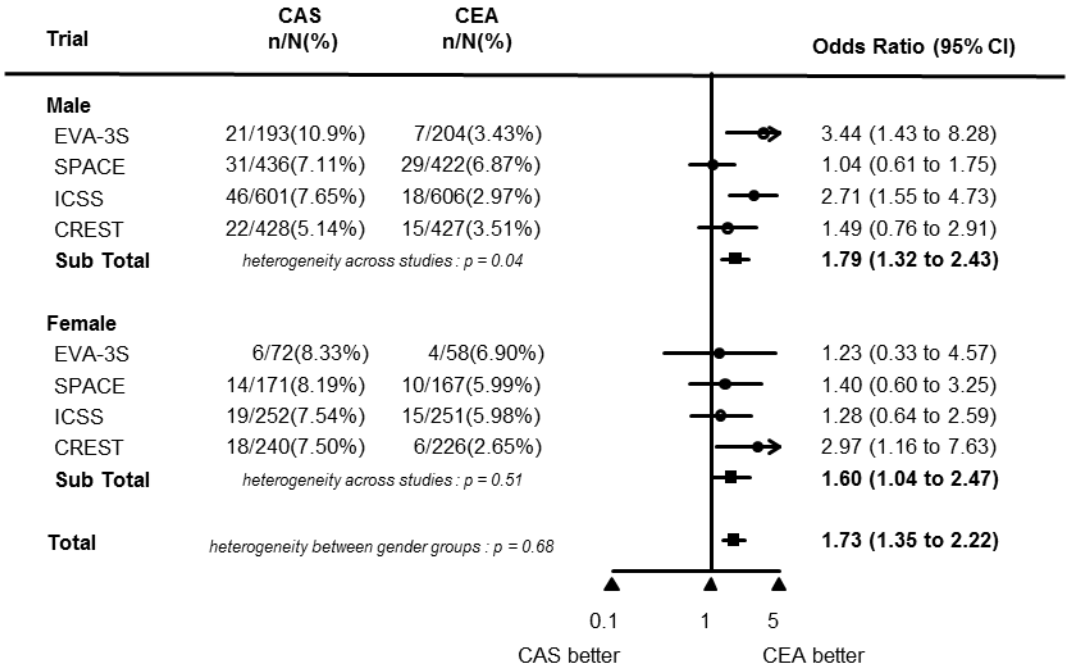
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.2: PROCEDURAL STROKE OR DEATH risks in RCTs comparing CAS vs CEA, by patient's age



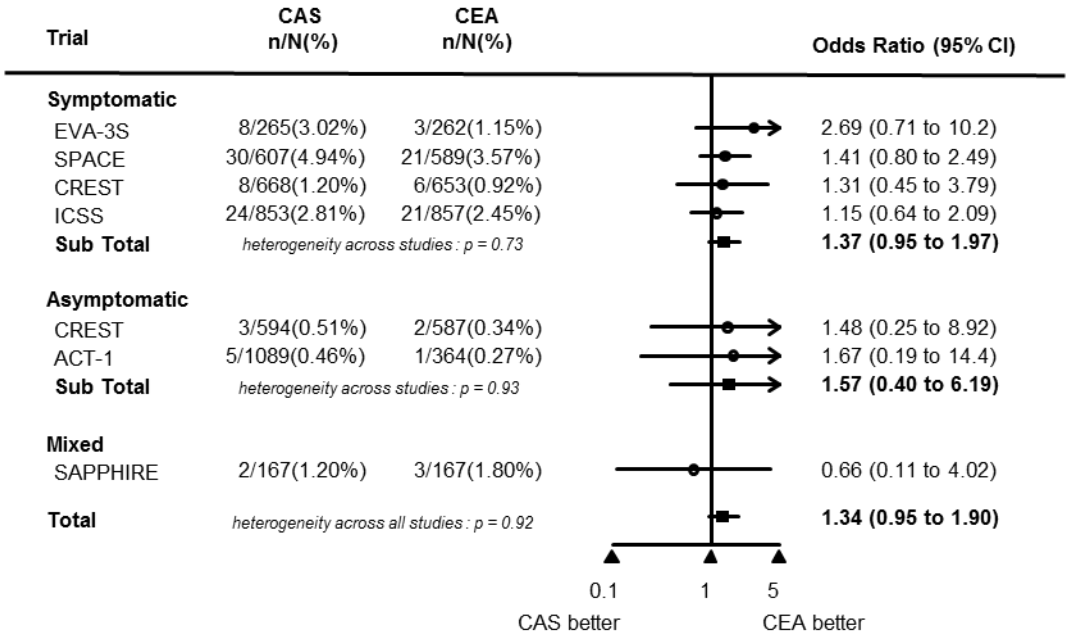
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.3: PROCEDURAL STROKE OR DEATH risks in RCTs comparing CAS vs CEA by patient's gender



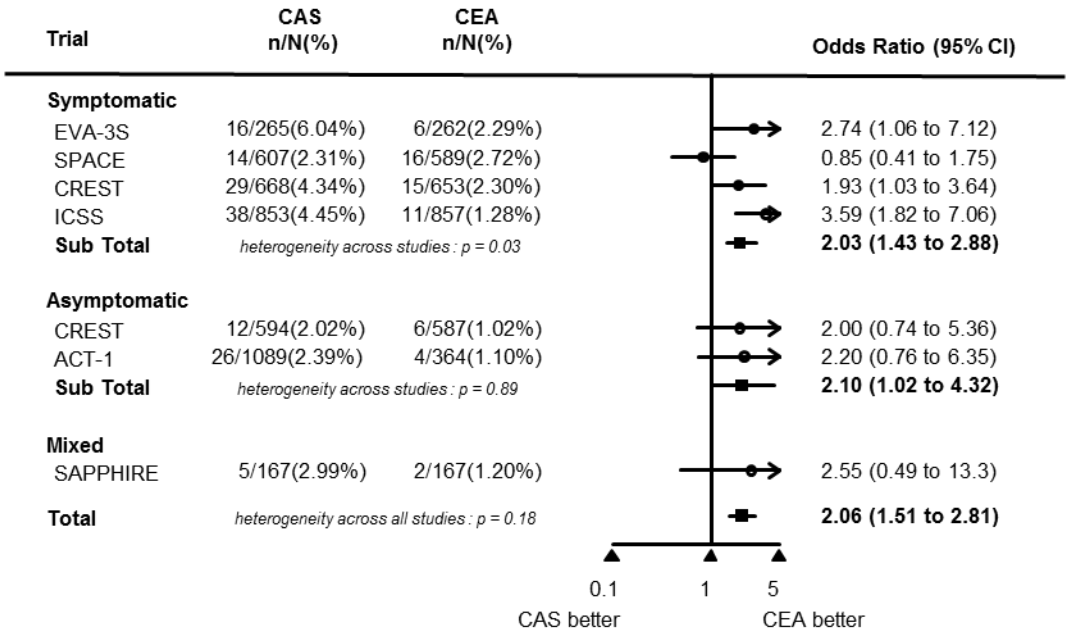
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.4: PROCEDURAL MAJOR STROKE risks in RCTs comparing CAS vs CEA



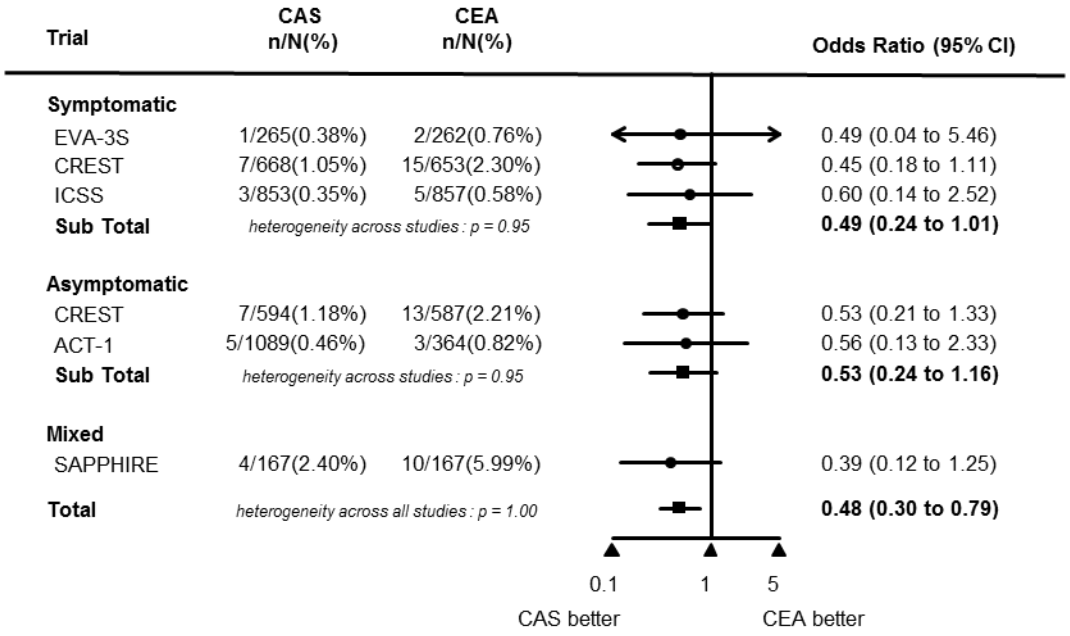
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Major stroke: Modified Rankin Score of ≥3

Appendix Figure 3.5: PROCEDURAL MINOR STROKE risks in RCTs comparing CAS vs CEA



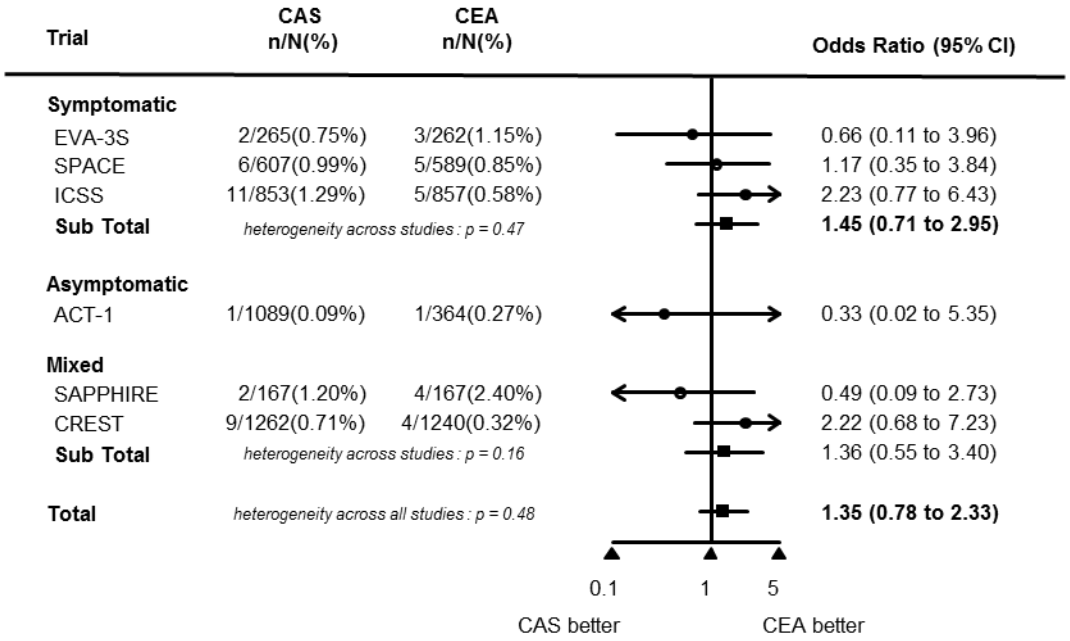
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Minor stroke: Modified Rankin Score of<3

Appendix Figure 3.6: PROCEDURAL MI risks in RCTs comparing CAS vs CEA



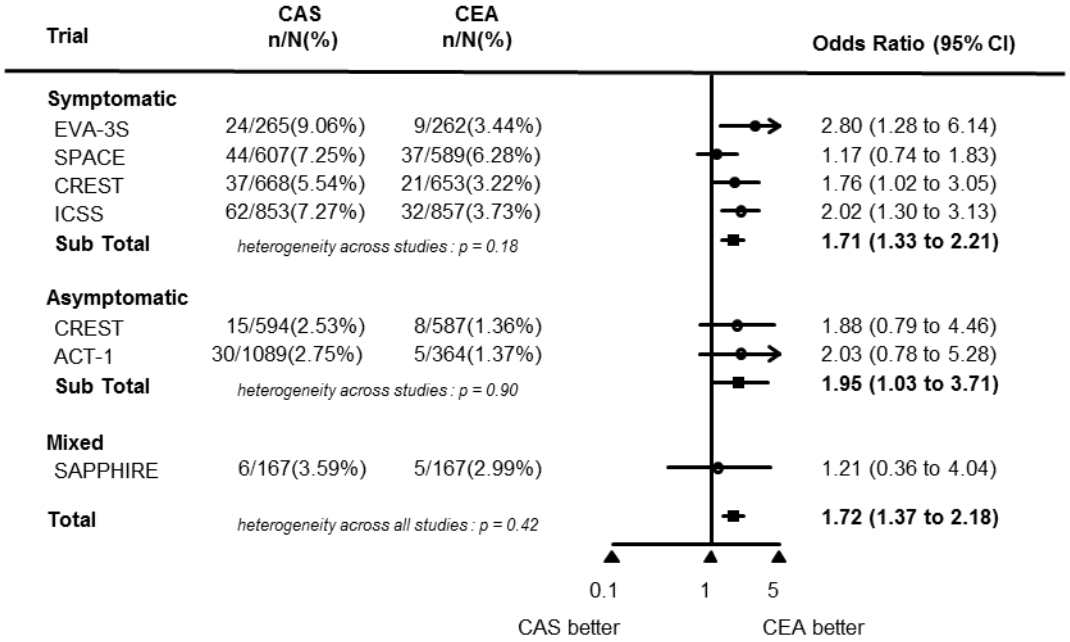
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.7: PROCEDURAL DEATH risks in RCTs comparing CAS vs CEA



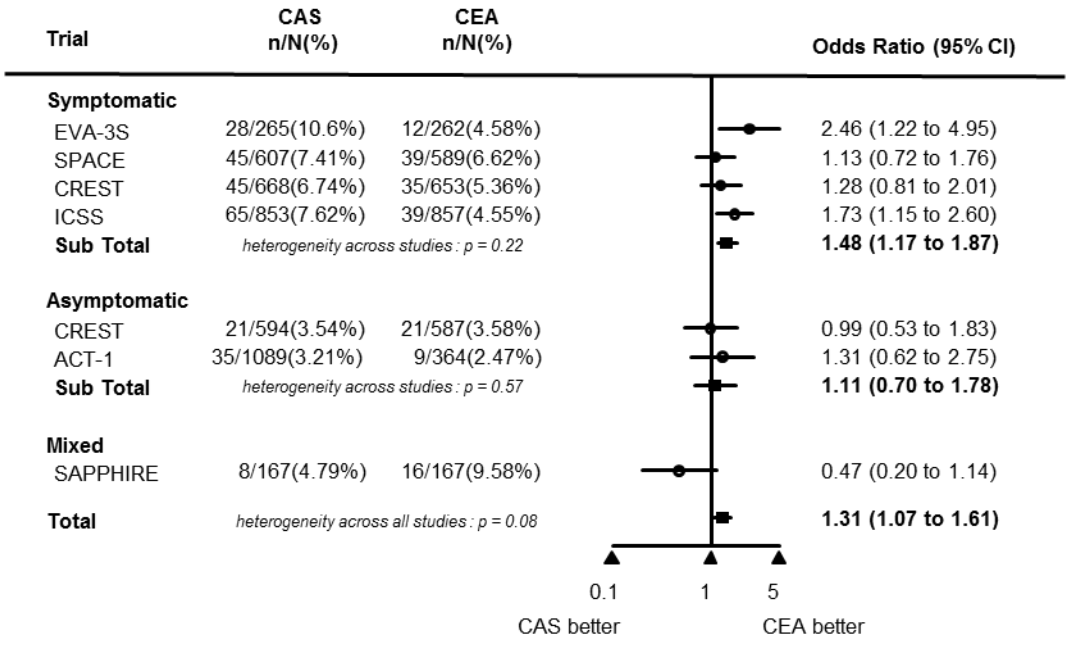
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.8: PROCEDURAL STROKE risks in RCTs comparing CAS vs CEA



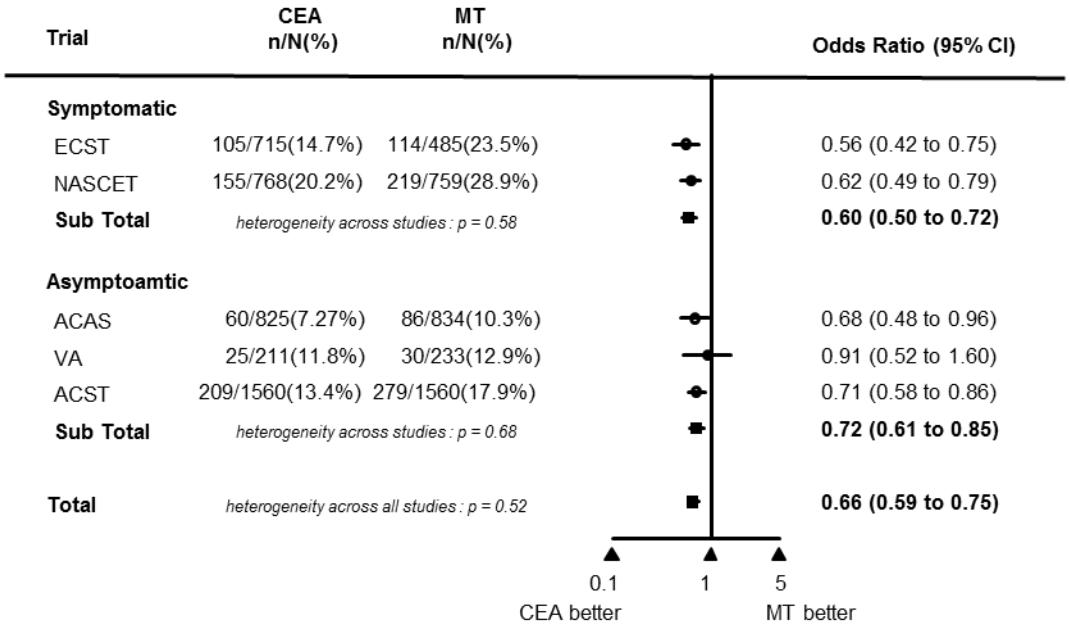
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.9: PROCEDURAL STROKE, DEATH, OR MI risks in RCTs comparing CAS vs CEA



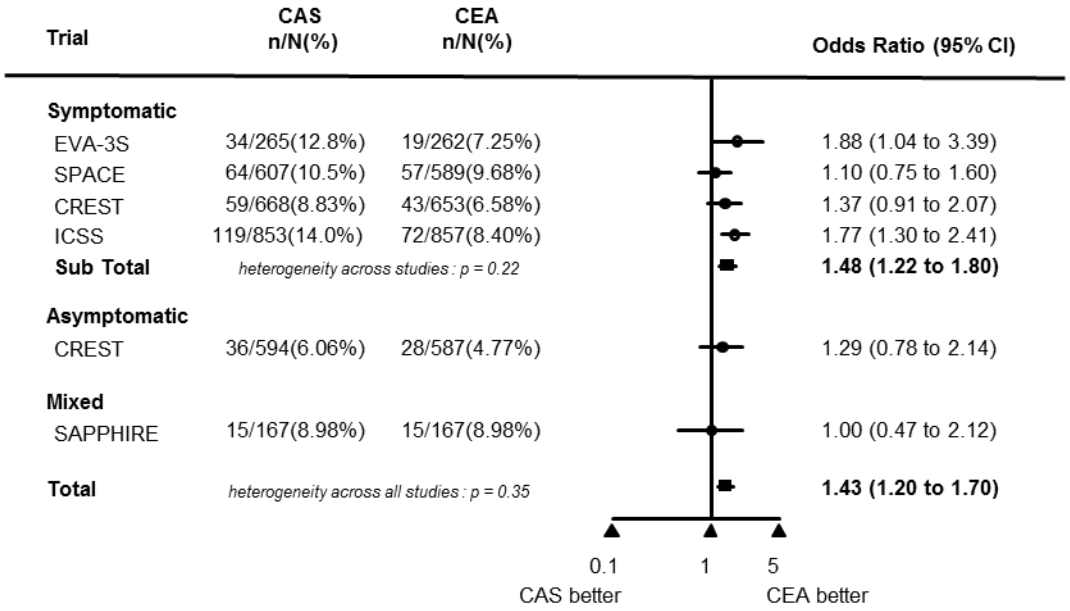
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.10: ANY STROKE OR PROCEDURAL DEATH* risks in RCTs comparing CEA vs MT



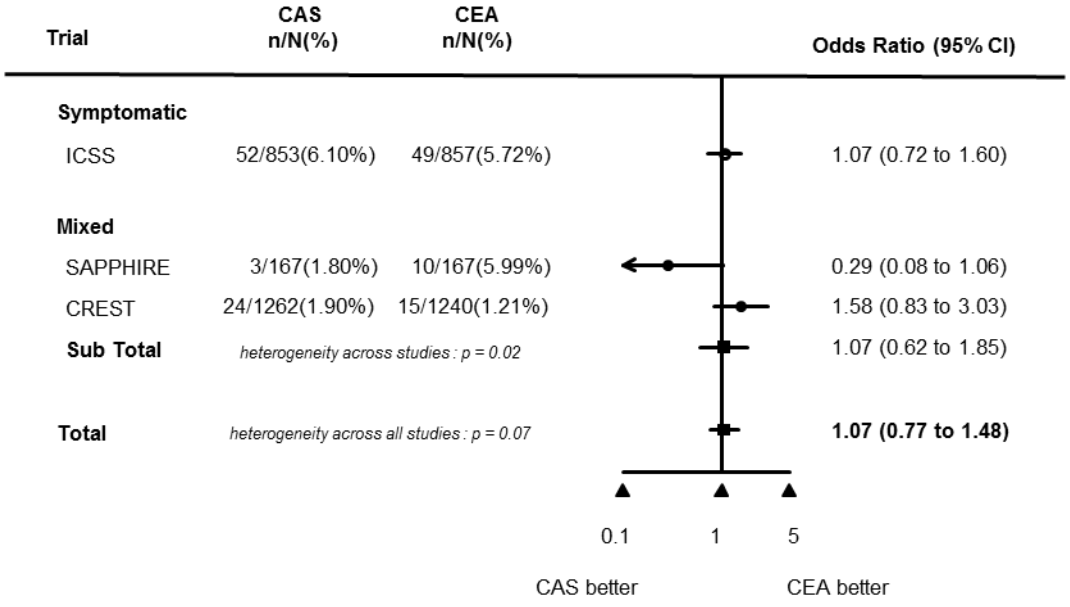
CEA: Carotid Endarterectomy; MT: Medical Therapy; *procedural deaths are those occurring within 30 days of trial surgery *with no procedural deaths in MT arms unless the patient randomized to MT underwent CEA and died within 30 days of surgery*

Appendix Figure 3.11: ANY STROKE risks in RCTs comparing CAS vs CEA



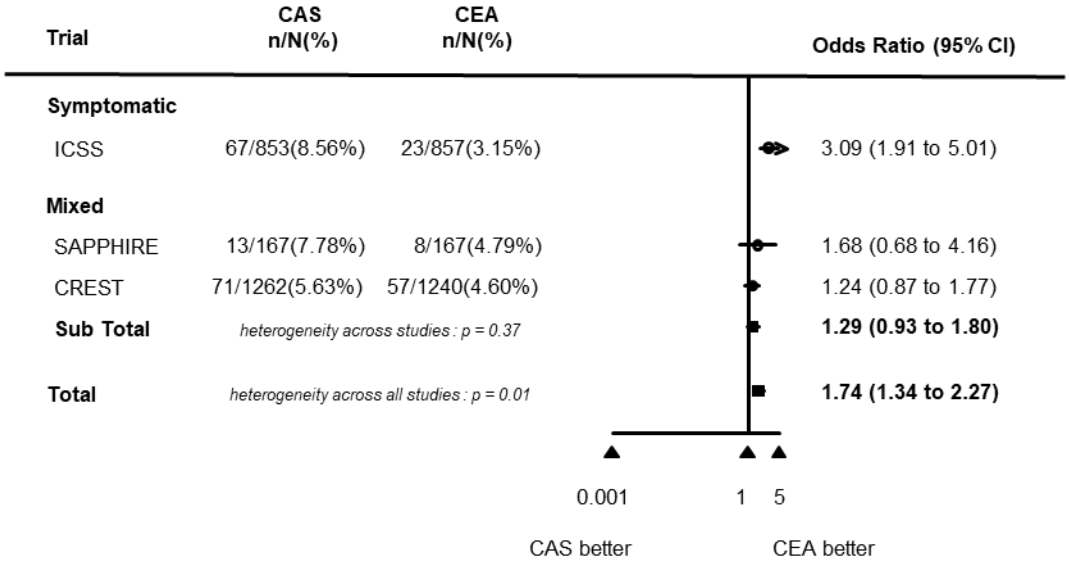
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.12: ANY MAJOR STROKE risks in RCTs comparing CAS vs CEA



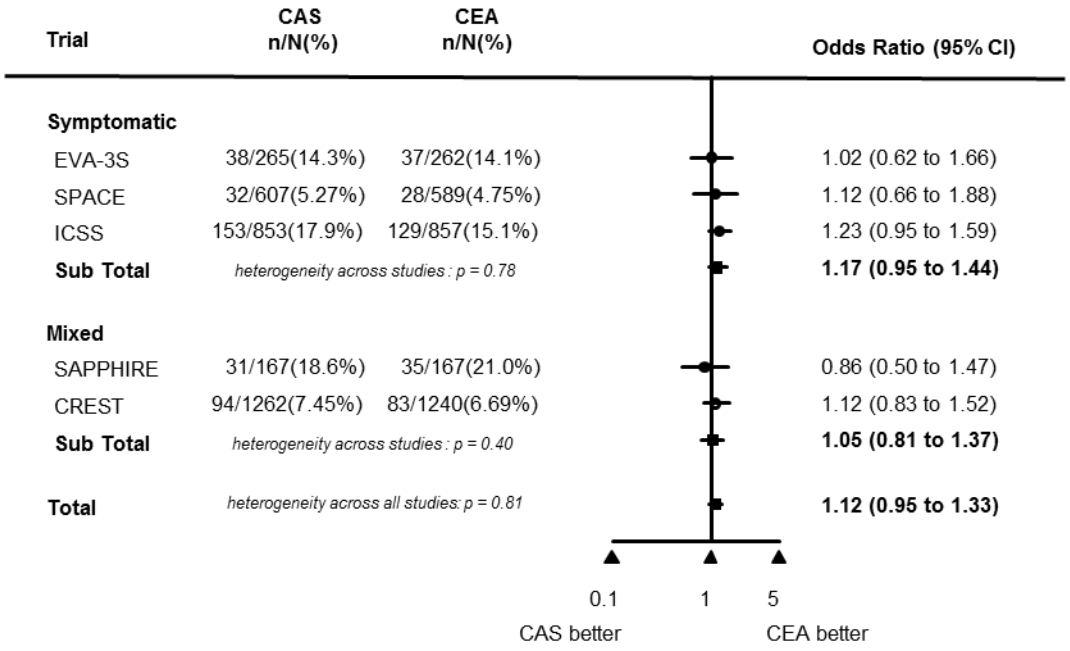
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Major stroke: Modified Rankin Score of ≥3

Appendix Figure 3.13: ANY MINOR STROKE risks in RCTs comparing CAS vs CEA



CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Minor stroke: Modified Rankin Score of<3

Appendix Figure 3.14: ANY DEATH risks in RCTs comparing CAS vs CEA



CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Table 3.1: Trials used in the network meta-analysis of any stroke or procedural death risks

RCT	Symptomatic Status	CEA		CAS		MT	
		Outcome*	n	Outcome*	n	Outcome*	n
NASCET	Symptomatic	155	768			219	759
ECST	Symptomatic	105	715			114	485
ACST	Asymptomatic	209	1560			279	1560
ACAS	Asymptomatic	60	825			86	834
VA	Asymptomatic	25	211			30	233
ICSS	Symptomatic	74	857	122	853		
EVA-3S	Symptomatic	20	262	35	265		
SPACE	Symptomatic	59	589	65	607		
CREST	Symptomatic	43	653	62	668		
CREST	Asymptomatic	28	587	36	594		

**Outcome: Any stroke or procedural death, with no procedural deaths in MT arms unless the patient randomized to MT underwent CEA and died within 30 days of surgery*

Appendix Table 3.2: PRISMA checklist

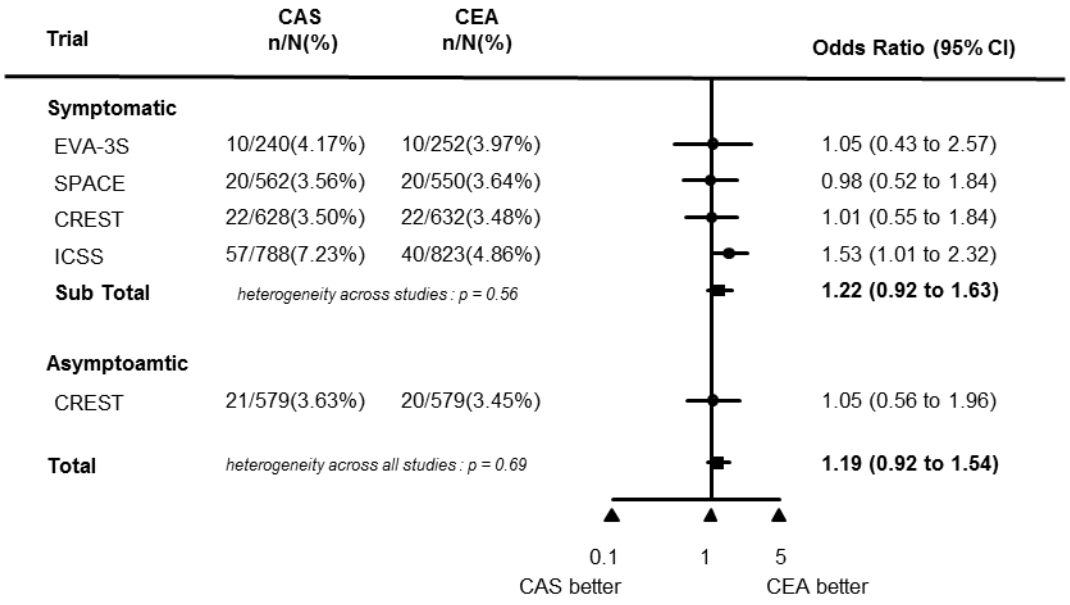
Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	60
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	62
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	62
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	61
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	61-62
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	61-62
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	61-62
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	N/A

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	N/A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	62-63
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	65
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	65

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	64-65
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	N/A
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	68-70
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	71-72
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	App fig 3.1 to 3.14
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	75, 78, 80
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	81

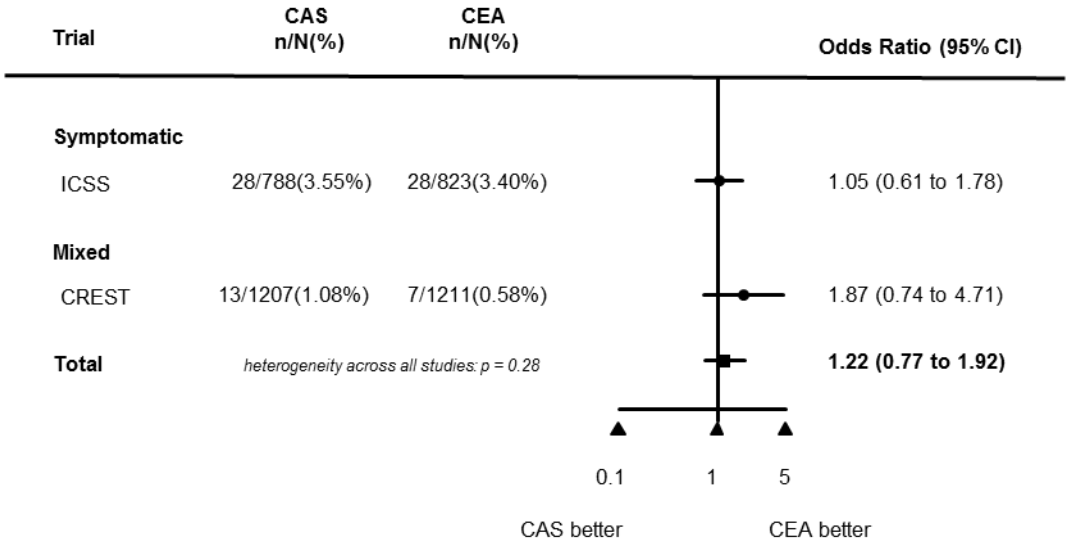
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	86-87
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	86, 87
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix Figure 3.15: POST-PROCEDURAL STROKE risks in RCTs comparing CAS vs CEA



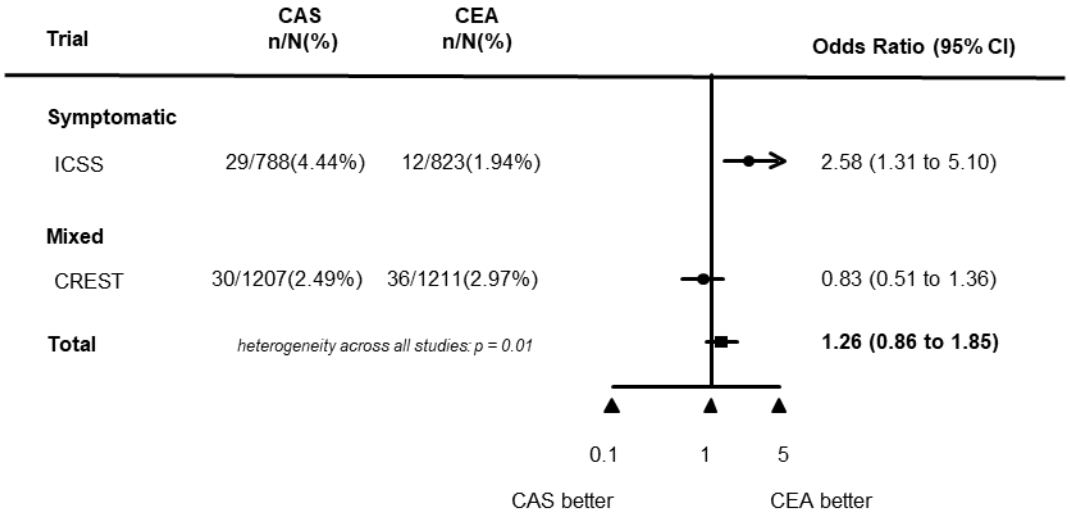
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Figure 3.16: POST-PROCEDURAL MAJOR STROKE risks in RCTs comparing CAS vs CEA



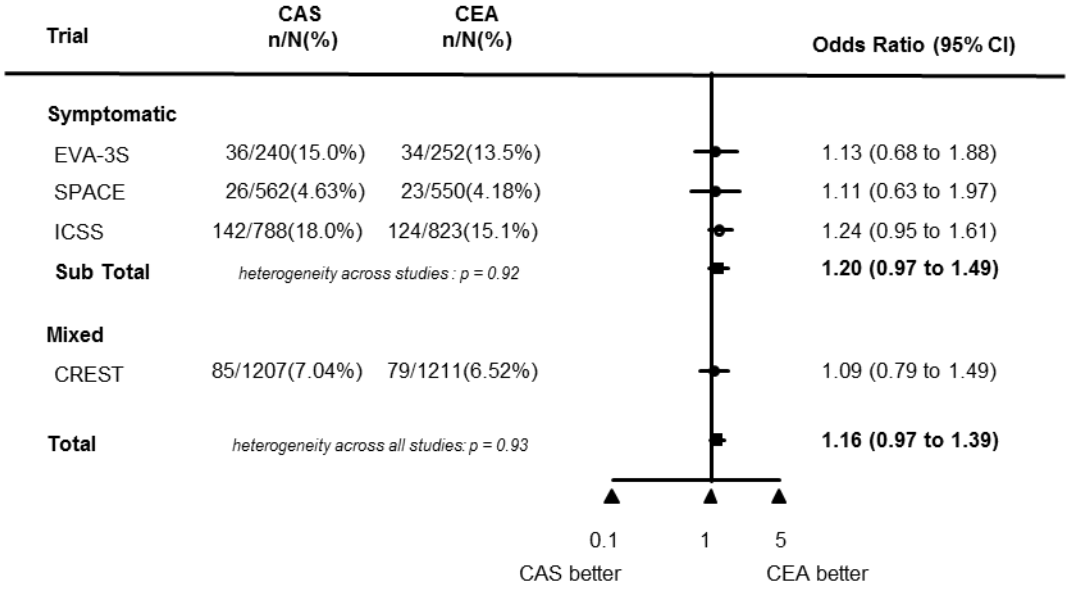
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Major stroke: Modified Rankin Score of ≥3

Appendix Figure 3.17: POST-PROCEDURAL MINOR STROKE risks in RCTs comparing CAS vs CEA



CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; Minor stroke: Modified Rankin Score of<3

Appendix Figure 3.18: POST-PROCEDURAL DEATH risks in RCTs comparing CAS vs CEA



CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix material for Chapter 4

Systematic review and meta-analysis of randomized evidence of procedural, post-procedural and overall effects of CEA and CAS

Appendix Table 4.1: Search strategy for observational cohort studies reporting procedural and/or long-term effects of CEA or CAS and number of hits in Medline and Embase

Search line	Search terms	Medline to 20th May 2016	Embase to 20th May 2016
#1	(Carotid ADJ3 Stenosis) OR (Carotid ADJ2 Artery)	70733	121349
#2	(Carotid ADJ2 Endarterectom*) OR CEA OR (Carotid ADJ2 Stent*) OR CAS OR (Carotid artery angioplasty and stent*)	87619	115939
#3	peri-procedur* OR peri procedur* OR periprocedur* OR procedur* OR operat* OR peri-operat* OR peri operat* OR perioperat* OR benefit* OR risk* OR complication* OR adverse event* OR adverse effect* OR mortality OR death* OR TIA OR survival OR stroke OR myocard* OR outcom*	6463904	8692914
#4	registr* OR audit OR database OR cohort OR popul* OR sample OR prospec*	2848305	3795897
#1 AND #2 AND #3 AND #4 (carried forward)		2618	3924

Note: All searches were performed for Keyword, which incorporates abstract and title

Appendix Text 4.1: Adapted Newcastle-Ottawa Scale for assessing quality of single-arm observational cohort studies

Note: A study can be awarded a maximum of 8 stars.

Selection:

1) Representativeness of the cohort (max 1 *)

- **a)** truly representative of the carotid stenosis patients in the community (*)
- **b)** somewhat representative of the carotid stenosis patients in the community (*)
- **c)** selected group of users eg nurses, volunteers
- **d)** no description of the derivation of the cohort – i.e no mean age; gender breakdown given

2) [Modified] Clear description of important determinants of procedural and long-term risk in cohort (max 2*)

- **a)** Age, gender, type of symptom (incl degree of stenosis), operator characteristics reported (*)
- **b)** Results presented for important subgroups of participants- by degree of stenosis, age, gender, type of symptom or operator characteristics (*)

3) Ascertainment of exposure: clear ascertainment of procedure performed/ medical therapy

- **a)** secure record (eg surgical records) (*)
- **b)** self-report
- **c)** no description

4) Demonstration that outcome of interest was not present at start of study: the outcome of interest is stroke however it is also the indication for procedure therefor clear description of symptomatic status needed.

- **a)** yes (*)
- **b)** no

Outcome:

1) Assessment of outcome

- **a)** Occurrence of death/stroke/MI well ascertained (record linkage) (*)

b) Occurrence of death/stroke/MI could have been missed (e.g. self-reported data)

2) Was follow-up long enough for outcomes to occur

a) yes (outcome ascertained in all participants at 30 days, follow-up duration of at least 2 years for long-term outcomes) (*)

b) no (e.g. follow-up less than 2 years for long-term outcomes; outcome not ascertained in all participants at 30 days)

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for(*)

b) subjects lost to follow up unlikely to introduce bias - small number (less than 5%) lost in follow up, or description provided of those lost (*)

c) Greater than 5% loss in follow-up and no description of those lost

Appendix Table 4.2: Studies excluded due to overlapping study population

Author	Study setting	Study period	Alternative manuscript used	Study period of alternative manuscript
De Rango P. (2010)**(43)**	Single Center - Uni of Perugia Hospital, Italy (Only Females)	Jan 2004 - Jan 2009	Parlani G. (2012)	Jan 2001 - March 2009
Dorigo W. (2009)**(44)**	Single Centre – Uni of Florence	Jan 1996 – Dec 2007	Dorigo W. (2011)	Jan 1996 – Dec 2008
Fairman R. (2007)**(45)**	CAPTURE	Oct 2004 – Mar 2006	Gray A. (2007)	Oct 2004 – March 2006
Go C. (2015)**(46)**	Single Centre – Division of Vascular Surgery, University of Pittsburgh	Jan 2000 – Dec 2007	Avgerinos D. (2014)	Jan 2000 – Dec 2008
Gray W. (2011)**(25)**	CAPTURE 2	Mar 2006 – Jan 2009	Gray A. (2009) and Chaturvedi S. (2010)	Mar 2006 – Jan 2009
Gray W. (2007)**(47)**	CAPTURE	Oct 2004 – Mar 2006	Gray A. (2007)	Oct 2004 – March 2006
Gupta P. 2013**(48)**	NSQIP	2005 - 2010	Bekelis K. (2013)	2005 - 2010
Halm E. (2005) **(49)**	Six Hospitals, New York City, USA	Jan 1997 – Dec 1998	Medicare Beneficiaries of New York – Halm E. (2009)	Jan 1998 – June 1999
Horner R. 2002**(50)**	VA centres	Oct 1994 – Sept 1997	Sidawy A. (2008)	1996-2003
Jeffrey J. (2011)**(51)**	SVS Vascular Registry	Until Oct 2009	Jeffrey J. (2014)	Until 2011
Jeffrey J. (2012)**(52)**	SVS Vascular Registry	Until Dec 2010	Jeffrey J. (2014)	Until 2011
Kapral M. (2003)**(53)**	CEAs performed in Ontario, Canada	1994 - 1997	Tu J. (2003)	Jan 1994 – Dec 1997
Kragsterman B. (2004)**(54)**	SWEDVASC	Jan 1994 – Dec 1996	Kragsterman B. (2006)	1994 - 2003

Author	Study setting	Study period	Alternative manuscript used	Study period of alternative manuscript
Kragsterman B. (2006)**(55)**	SWEDVASC	1994 - 2003	Kragsterman B. (2006)	1994 - 2003
Matsumura J. (2010) **(56)**	CAPTURE 2	March 2006 – Jan 2009	Gray A. (2009) and Chaturvedi S. (2010)	Mar 2006 – Jan 2009
Menyhei G. (2011) **(57)**	VASCUNET	Jan 2003 – Dec 2007	Paper does not define procedural time period. Study population repeated in Vikatmaa P. (2012) with better definition of procedural time frame.	2005 - 2010
Pieniążek P. (2012) **(58)**	TARGET-CAS	2002 - 2010	Dzierwa K. (2013)	Jan 2001 – Feb 2011
Press M. (2006) **(59)**	Six Hospitals, New York City, USA	Jan 1997 – Dec 1998	Medicare Beneficiaries of New York – Halm E. (2009)	Jan 1998 – June 1999
Rockman C. (2005)**(60)**	New York University Medical Centre	1992 - 2000	Rockman C. (2006)	1992-2003
Schermerhorn M. (2013)**(61)**	SVS Vascular Registry	Nov 2000 – Sept 2011	Jeffrey J. (2014)	Until 2011
Sidawy A. (2009)**(62)**	SVS Vascular Registry	Until Dec 2007	Jeffrey J. (2014)	Until 2011
Stoner M. (2006)**(63)**	VA NSQIP	2000 - 2003	Sidawy A. (2008)	1996-2003
Upchurch G. (2014)**(64)**	SVS Vascular Registry (limited to patients with contralateral carotid occlusion	Jul 2005 – Dec 2011	Jeffrey J. (2014)	Until 2011
Wallaert, J. (2012)**(65)**	National Surgical Quality Improvement Program (NSQIP)	2007 - 2009	Bekelis K. (2013), Garg J. (2011), Wu T. (2015)	2005-2010; Jan 2005 – Oct 2009; 2005 - 2012
White R. (2010)**(66)**	SVS Vascular Registry (only CAS)	Until Nov 2008	Jeffrey J. (2014)	Until 2011

Author	Study setting	Study period	Alternative manuscript used	Study period of alternative manuscript
Wholey, M. (2000)**(67)**	Global CAS Registry	1997 - 1999	Wholey M. (2003)	June 1997 – Sept 2002

Appendix Table 4.3: Characteristics of observational studies of outcomes of carotid endarterectomy (CEA) or carotid artery stenting (CAS)

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Assadian A. (2005)**(68)** Single Centre - Vienna, Austria	CEA	1355 CEAs: 58.8% male, 41% asymptomatic, Mean Age: 70.5 years	Jan 1996 – Dec 2002	30 days from procedure	Symptomatic patients and asymptomatic patients; degree not stated	Symptomatic – patients have had a prior Stroke or TIA	Procedural: Death, Stroke	Not reported
Avgerinos D. (2015)**(69)** Single Centre – Division of Vascular Surgery, University of Pittsburgh	CEA	1342 CEAs: 55.6% male; 64.7% asymptomatic; Mean age: 71.2	Jan 2000 – Dec 2008	Mean of 55 months	Symptomatic and asymptomatic; degree of stenosis not stated	Symptomatic – experienced neurological ischemic events such as TIA, amaurosis fugax, or stroke, 6 months before CEA	Procedural: Death, Stroke, Stroke/Death, MI	Social security death index used to record deaths
Ballotta E. (2014)**(70)** Single Centre – Padova, Italy	CEA	2007 CEAs (1773 patients): 70.6% Male; 27.9% Asymptomatic; Mean Age: 75.2	Jan 1990 – May 2012	Median: 11.2 years	Symptomatic patients and asymptomatic patients; degree not specified	Not reported	Procedural: Death, Stroke, Major Stroke, Minor Stroke, Stroke/Death Long-term:	By a consultant neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
							Death, Stroke, Ipsi Stroke, Contra Stroke (none by Symp status)	
Bekelis K. (2013)**(71)** NSQIP database, USA	CEA	35 698CEA patients: 5% Male; 56.1% Asymptomatic; Mean Age: 71.1	2005-2010 Follow-up: 30 days from procedure.	30 days from procedure	Symptomatic and asymptomatic patients; degree not specified	Symptomatic- any subject with a history of cerebrovascular accident with or without neurological deficit or a history of TIA. 63.1% TIA; 35% Stroke	Procedural: Death, Stroke, MI, Stroke/Death/MI	By a trained nurse
Bosiers M. (2007)**(72)** AZ St-Blasius, Dendermonde, Belgium; Imelda Hospital, Bonheiden, Belgium; University of Sienna, Italy;	CAS	3179 CAS patients: 58.6% Asymptomatic; Mean Age: 72	Not reported	30 days from procedure.	Symptomatic and Asymptomatic; degree of stenosis not stated	Not reported	Procedural: Stroke/Death/TIA	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Villa Maria Cecilia Hospital, Cotignola, Italy								
Bosiers M. (2005)**(73)** ELOCAS Registry – Four high-volume European centres	CAS	2172 CAS patients (7 technically unsuccessful): 58.4% Asymptomatic; Mean Age: 71	Feb 1993- Dec 2004	5 years	Symptomatic and asymptomatic patients; degree not specified	Not reported	Procedural: Major Stroke/Death Long-term: Stroke/Death	By an independent team of neurologists
Calvillo-King L. (2010)**(74)** New York Carotid Artery Surgery Study – All Medicare beneficiaries who underwent in New York State, USA	CEA	6553 CEA patients: 54.9% Male; 100% Asymptomatic; Mean Age: 74.5	Jan 1998 – June 1999	30 days from procedure.	Asymptomatic patients; degree not specified	Asymptomatic patients were defined as those with no history of carotid stroke or TIA <= 12 months before surgery Not reported	Procedural: Stroke, Death, Stroke/Death	Identified by medical records – major outcomes reviewed by 2 study physicians (including a neurologist)

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Chaturvedi S. (2010)**(75)** CAPTURE 2 – 186 clinical sites in the USA Conflicts – Abbott Vascular	CAS	5297 CAS patients: 61.7% Male; 85.3% Asymptomatic; Mean Age: 72.3	Until Jan 2009 Follow-up: 30 days	30 days from procedure.	Symptomatic (>=50%) and asymptomatic (>=80%) patients	Symptomatic patients- ipsilateral hemispheric stroke, TIA, and/or amaurosis fugax within the previous 180 days. Not reported	Procedural: Death, Stroke, MI, Major Stroke, Minor Stroke, Ipsi Stroke, Non-ipsi stroke, Death/Stroke, Death/Stroke/MI, Death/Major Stroke	By an independent neurologist
Cremonesi A. (2009)**(76)** Villa Maria Cecilia Hospital, Cotignola, Italy	CAS	1523 CASs (1380 CAS patients) 72.4% Male; 75.9% Asymptomatic; Mean Age: 71.9	April 1999 – Sept 2007	12 months, afterwards through phone interviews (Asymp– 107 months, Symp-97 months)	Symptomatic (>=50%)and asymptomatic (>=80%) patients	Symptomatic- a lesion related neurological event in the preceding 6 months. 43.7% TIA, 40.7% stroke, 15,5% Amaurosis fugax	Procedural: Stroke/Death, Major Stroke/ Death, Minor Stroke Long-term: 30 day stroke/death plus stroke/stroke related death beyond 30 days	Self-reported by patient
De Rango P. (2011)**(77)**	CAS	1083 CAS patients: 75.3% Asymptomatic; Mean Age: 71.6 years;	Jan 2004 – Mar 2009	30 days from procedure.	Symptomatic patients (> 70% stenosis) & asymptomatic patients (> 70% stenosis) by	Patients were defined symptomatic when ipsilateral hemispheric or retinal symptoms	Procedural: Stroke/Death	In the presence or suspicion of new neurological or

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Single Centre study - Perugia, Italy		71% Male			Duplex ultrasound & confirmed at angiography.	occurred within 6 months from the procedure. Not reported		cardiac events, a team of neurologists and cardiologists was routinely consulted and documented the presence.
Dorigo W. (2011)**(78)** Single Institution – Uni of Florence, Italy	CEA	4305 CEAs (3573 patients): 65.8% Asymptomatic; 68.8% Male Mean Age (Diabetics): 71.3 yrs; Mean Age (Non-Diabetics): 71.7 yrs	Jan 1996 – Dec 2008	Mean: 40 months	Symptomatic and Asymptomatic; degree of stenosis not stated - NASCET	Patients were considered to be asymptomatic in the absence of neurological symptoms (TIA or stroke) within 6 months from the intervention 59.2% TIA, 15.5% Stroke, 25.3% Veretrobasilar	Procedural: Stroke/Death Long-term: Death, Stroke (not by Symp status)	By an independent neurologist
Dzierwa K. (2013)**(79)** Single Centre - Krakow, Poland	CAS	1252 CASs (1139 patients): 44.6% Asymptomatic; 68.9% Male Mean Age: 66.3 yrs	Jan 2001 – Feb 2011	30 days from procedure.	Symptomatic (>50%) and Asymptomatic (>=80%) - Doppler Duplex ultrasound & computed tomography angiography	Symptomatic- history of TIA, amaurosis fugax or stroke ipsilateral to the ICA stenosis up to 6 months before intervention Not reported	Procedural: Death, Stroke, Major Stroke, Minor Stroke, Stroke/Death (by addition)	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Egashira Y. (2014)**(80)** Japan using Japanese Registry of Neuroendovascular Therapy	CAS	5191 CAS: 86.6% male; 40.7% asymptomatic; Mean age: 71.6	Jan 2008 – Dec 2009	30-day follow-up	Symptomatic and asymptomatic; degree of stenosis not stated	Not reported	Procedural: Stroke	Not reported
Garg J. (2011)**(81)** National Surgical Quality Improvement Program (NSQIP)	CEA	9285 CEAs: 57.3% Male; Mean Age: Academic Hos – 70.8, Comm Hos – 71.8;	Jan 2005 – Oct 2009	30 days from procedure	Symptomatic patients and asymptomatic patients; degree not stated	Not reported	Procedural: Death, Stroke/Death, Stroke/Death/MI	Data entered by trained clinical nurse reviewers
Goode S. (2013)**(82)** UK CAS Registry; 31 hospitals in the UK	CAS	1154 CAS patients: 17% Asymptomatic; Asymp Male: 74.1% Symp Male: 67.2%	1998-2010	Up to 7 years	Symptomatic and Asymptomatic; <90% of patients have degree of stenosis >50%	Not reported	Procedural: Death, Stroke/Death, Stroke/Death/MI, Disabling Stroke, Non-disabling stroke, MI Long-term: Death	Not reported for 30 day outcomes; self-reported for long-term outcome through follow-up form. If form not received then another form sent, and afterwards patients were contacted by telephone.

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Gray A. (2007)**(83)** CAPTURE Registry, 144 sites, United States Study Sponsor - Abbott Vascular	CAS	3500 CAS patients: 61.1% Male; 86.2% Asymptomatic; Mean Age: 72.7	Oct 2004 – March 2006	30 days from procedure.	Symptomatic patients (>= 50% stenosis) and asymptomatic patients (>= 80% stenosis)	Not reported	Procedural: Death, Stroke, Major Stroke, Minor Stroke, MI, Death/Stroke, Death/Major Stroke, Death/Stroke/MI	By two independent neurologists
Gray W. (2009)**(84)** CAPTURE-2 and EXACT studies Conflicts – Abbott Vascular	CAS	CAPTURE 2: 4175 CEA patients: 61.7% Male; 86.9% Asymptomatic; Mean Age: 72.5 EXACT 2: 2145 CEA patients: 63.1% Male; 90.1% Asymptomatic; Mean Age: 72.9	EXACT: Nov 2005-April 2007 CAPTURE 2: Mar 2006 – Not reported	30 days from procedure.	Symptomatic (>=50%) and asymptomatic (>=80%) patients	Symptomatic-experienced TIA, amaurosis fugax, or stroke in the territory supplied by the target vessel within 180 days previous to procedure Not reported	Procedural: Death/Stroke, Death/Major Stroke	By an independent neurologist
Halm E. (2009)**(85)** New York Carotid Artery Surgery Study – All Medicare	CEA	9308 CEAs: 55.7% Male; 71.5% Asymptomatic; Mean Age: 74.6	Jan 1998 – June 1999	30 days from procedure.	Symptomatic and asymptomatic patients; degree not specified	Patients without neurological symptoms referable to a carotid artery distribution in the 12 months before surgery were defined as asymptomatic.	Procedural: Stroke/Death	Identified by medical records – major outcomes reviewed by 2 study physicians (including a neurologist)

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
beneficiaries who underwent in New York State, USA						66.4% TIA, 27% Minor stroke, 5.42% Major stroke, 13.33% Acute syndromes		
Hamdan A. (1999)**(86)** Beth Israel Deaconess Medical Center, Boston, Massachusetts , USA	CEA	3092 CEAs (2714 patients): 60.7% Male; 42.6% Asymptomatic; Mean Age: Normal renal func: 70.1 Not-normal renal func: 71.5	Jan 1990 – Aug 1997	30 days from procedure.	Symptomatic and asymptomatic patients; degree not specified	Symptomatic- TIA, episodes of amaurosis fugax, and completed stroke Not reported	Procedural: Stroke	Not reported
Hopkins L. (2014)**(87)** CABANA study, 99 US centers Sponsor - Boston Scientific Corporation.	CAS	1097 CAS patients 67.3% Male; 4% Asymptomatic; Mean Age: 71.3	Dec 2008 – Oct 2010	30 days from procedure.	Symptomatic patients (>= 50% stenosis) and asymptomatic patients (>= 80% stenosis) by ultrasound or angiography (NASTEC)	Not reported	Procedural: Death, Stroke, Major Stroke, Minor Stroke, Ipsi, Contra, MI, Stroke/Death/MI	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Jalbert J. (2015)**(88)** Medicare beneficiaries at least 66 years old	CAS	22516 CAS patients: 60.5% male, 47.4% asymptomatic, Mean Age: 76.3 years	2005 - 2009	Mean of 2 years	Symptomatic and Asymptomatic; degree of stenosis not stated	Not reported	Procedural: Death	Record linkage
Jeffrey J. (2014)**(89)** SVS Vascular Registry	CEA CAS	3373 CAS patients: 1841 Asymptomatic; 60.6% Males ; Mean Age Male:71.2; Female: 71.2 6491 CEA patients: 4038 Asymptomatic; 58.8% Males; Mean Age Male:70.7; Female: 71.0	2005 -	30 days from procedure	Degree of stenosis CEA: 98 (male) ;99% (female) CAS: 69 (male);74% (female) on average	Not reported	Procedural: Death, Stroke, MI, Death/Stroke/MI.	Analysis based on only patients who had 30 day follow-up visits
Kragsterman B. (2006)**(90)** Swedvasc, All centres, Sweden	CEA	6169 CEAs (5808 patients):Mean Age: 70; 66.2% Male; 10.8% Asymptomatic	1994-2003	10 years	Symptomatic and Asymptomatic; degree of stenosis not stated	Asymptomatic stenosis excluded all ipsilateral carotid artery events & non-hemispheric symptoms within 6 months Not reported	Procedural: Stroke/Death, Death, Fatal Stroke Long-term: Death	Not reported for procedural outcomes. Long-term death through record linkage with National Population Registry

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Kresowik T. (2014)**(91)** 10 states in the USA (Arkansas, Georgia, Illinois, Indiana, Iowa, Kentucky, Michigan, Nebraska, Ohio, Oklahoma)	CEA	19690 CEAs: 40.5% Asymptomatic	1995-1996 1998-1999	30 days from procedure	Symptomatic and Asymptomatic; degree of stenosis not stated	Not reported	Procedural: Death, Stroke/Death	Record linkage and reviewed by 2 independent clinicians
Kucey D. (1998)**(92)** 8 participating centresm Canada	CEA	1280 CEAs: 27.3% Asymptomatic; 66.1% Male; 23.1% > 75 years	Jan 1994 – Dec 1996	30 days from procedure	Symptomatic and Asymptomatic; defined by NASCET criteria	Symptomatic - Ipsilateral hemispheric or ocular event within 120 days of the surgery 40.2% TIA, 5% Moderate Stroke, 34% Minor stroke, 4.15% Amaurosis fugax	Procedural: Death, Stroke/Death, Non-fatal Stroke	From patient charts
Lindstrom D. (2012)**(93)** Swedvasc registry	CEA CAS	258 CAS patients: 42% Asymptomatic; Mean Age: 69; 74% Male 6474 CEA patients: (79%) symptomatic	Nov 2004 - April 2011	30 days from procedure	Symptomatic and asymptomatic patients; degree of stenosis not stated	Symptomatic stenosis was defined as all ipsilateral carotid artery events within 180 days prior to the intervention.	Procedural: Stroke/Death	Not reported

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
						Not reported		
Long W. (2007)**(94)** Single Centre – William Beaumont Hospital, Royal Oak, MI, USA	CEA	1972 CEAs: 59% Male; 63% Asymptomatic; Mean Age: 72.1	Jan 1999 – Dec 2003	30 days from procedure	Symptomatic patients and asymptomatic patients; degree not stated	Not reported	Procedural: Death, Stroke	Not reported
Lubke T. (2015)**(95)** Single Centre - University Hospital of Cologne, Germany	CEA	1880 CEAs 68.7% Male; 75.7% asymptomatic; Mean Age: 69.9 (Female) 68.7 (Male)	Jan 2000 – Dec 2010	11 years	Symptomatic and Asymptomatic; degree of stenosis not stated	Not reported	Procedural: Death, Stroke, Stroke/Death Long-term: Death	By the consultant neurologist
Lutz. H (2008)**(96)** Two teaching hospitals – Giessen and Dessau, Germany	CEA	1341 CEA patiens: 41.8% Asymptomatic; 73.2% Male; Mean Age GA: 66.5; Mean Age LA: 68.4	Jan 1995 – Dec 2004 Follow-up: 30 days	30 days from procedure.	Symptomatic (>70%)and asymptomatic (>80%) patients	Symptomatic – a clear statement of any ipsilateral neurologic deficit in the last six months 52.8% TIA, 38.3% Stroke	Procedural: Stroke (assumed as post-operative neurological event)	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Massop D. (2009)**(97)** SAPPHIRE Worldwide Registry	CAS	2001 CAS patients: 72.3% asymptomatic; Mean Age: 72.2; 62% Male	Jan 1989 – Dec 1998	30 days from procedure.	Symptomatic (>=50%) and Asymptomatic (>=80%) by ultrasound or angiogram	Symptomatic - TIA or stroke within 180 days of the procedure Not reported	Procedural: Stroke/Death	By an independent clinical events committee
Mattos A. (2001)**(98)** Southern Illinois University School of Medicine, USA	CEA	1249 CEAs (1113 patients): 75.3% Asymptomatic; Mean Age (women): 68.5 years; Age (men):68 years; 61% Male	Mar 1976 – Oct 1997	Mean (women): 48.6 months Mean (men): 50.9 months	Symptomatic (> 50% NASCET in 92% women and 95% men) & asymptomatic patients (> 60% ACAS in 99% women and 98% men)	Not reported	Procedural: Death, Stroke (by Gender subgroup)	Clinic charts, hospital records, referring physicians, telephone conversations with patients
Palombo D. (2009)**(99)** Italian Vascular Registry – 89 centers in Italy	CEA	5809 patients (5962 CEAs): 68.7% male, 68.2% asymptomatic, Mean Age: 72.7 years	Jan 2007 – Dec 2007	30 days from procedure	Symptomatic patients and asymptomatic patients; degree not stated	Not reported	Procedural: Stroke	Not reported
Parlani (2012)**(100)**	CEA CAS	2196 procedures: 71% Male; Mean Age: 71.3 years; 31.1% Symptomatic	Jan 2001 - March 2009	6 year follow-up	Symptomatic (>60%) and Asymptomatic (>70%)	Patients were defined as symptomatic when ipsilateral hemispheric or retinal symptoms	Procedural: Stroke/Death	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Single Centre - Hospital S. M. Misericordia, Perugia, Italy		1116 CEAs;416 Symptomatic; 70.9% Male 1080 CAS; 268 Symptomatic; 71% Male;		Mean follow-up: 47.23 months		occurred within 6 months from the procedure Not reported	Long-term: Death, Ischemic Stroke (Not by Symp status)	
Pulli R. (2005)**(101)** Single Centre – Firenze, Italy	CEA	1883 CEAs (1554 CEA patients): 52.1% Asymptomatic; Mean Age 70 years; 69.9% Male	1996-2001	3 years after procedure	Symptomatic and Asymptomatic; degree of stenosis > 70 in 99.4% of cases	Patients with nonhemispheric symptoms were considered to be asymptomatic Not reported	Procedural: Stroke/Death	Not reported
Reed A. (2003)**(102)** Brigham & Women's Hospital, Boston, USA	CEA	1370 CEAs (1184 patients): 57% Male; 54% Asymptomatic; Mean Age: Not reported	Jan 1990 – Dec 1999	30 days from procedure.	Symptomatic and asymptomatic patients; degree not specified	Not reported	Procedural: Death, Stroke , Stroke/Death	Not reported
Rockman C. (2005)**(103)**	CEA	1972 CEAs: 57.2% Male; 71.3% Asymptomatic; Mean Age: 72.3	Jan 1997 – Dec 1998	30 days from procedure.	Symptomatic and asymptomatic patients; degree not specified	Not reported	Procedural: Stroke	Through inpatient results and surgeons post-discharge office records. Two separate and

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Six hospitals, New York, USA								impartial investigators, including a neurologist, independently reviewed the medical records of all patients
Rockman C. (2006)**(104)** New York Uni Medical Centre, USA	CEA	1046 CEAs: 0% Asymptomatic; Mean Age: Not reported; 60.3% Male	1992-2003	30 days from procedure	Symptomatic patients only selected; degree of stenosis not stated	Preoperative symptoms were categorized as either hemispheric TIA (including amaurosis fugax) or completed stroke by clinical presentation and the results of brain imaging studies, when available. Early CEA: 69.9% TIA, 30.1% Stroke Late CEA: 52.9% TIA, 47.1% Stroke	Procedural: Death, Stroke, MI	Not reported
Schreiber T. (2010)**(105)**	CAS	1492 CAS patients: 78.2% Symptomatic; Mean Age 73.4 years; 62.7% Male	Aug 2003 – Oct 2005	1 year	Symptomatic patients (>= 50% stenosis) and asymptomatic patients (>= 80% stenosis) by ultrasound or angiogram	Not reported	Procedural: Stroke/Death	By an independent neurologist

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
CASES-PMS Study, 73 sites, USA Study Sponsor- Cordis Corporation								
Šedivý P. (2015)**(106)** Single Centre – Na Homolce Hospital, Czech Republic	CEA CAS	5363 CEAs: 46.7% Asymptomatic	1993 – 2014	30-day follow-up	Symptomatic and asymptomatic; degree of stenosis not stated	Not reported	Procedural: Stroke/Death	Not reported
Setacci C. (2010)**(107)** Single Centre study - Sienna, Italy	CAS	2124 CAS patients: Mean Age: 76.3; 65% Male; 48% Symptomatic	Dec 2000 – May 2009	30 days from procedure.	Symptomatic patients (> 70% stenosis) and asymptomatic patients (> 70% stenosis) by Doppler ultrasound	Not reported	Procedural: Stroke	By an independent neurologist
Sidawy A. (2008)**(108)** Veterans Affairs National Surgical Quality	CEA	20899 CEAs (20080 CEA patients): 50.2% Asymptomatic; Mean Age (GFR >=60, 30-59, M30): 66.7, 71.5, 71.9	Jan 1996 - Dec 2003	30 days from procedure in 79% and rest in-hospital	Symptomatic and Asymptomatic; degree of stenosis not stated	Symptomatic - Previous history of Stroke/TIA Not reported	Procedural: Death Stroke (a new cerebrovascular accident/ stroke or coma lasting 24 hours),	Recorded by trained nurse from medical record review, surgeon interview, or patient follow-up

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Improvement Program (VA-NSQIP) – 123 participating medical centres in the USA		Male Age (GFR >=60, 30-59, M30): 98.7%, 98.4%, 98.2% **GFR: glomerular filtration rate*					MI (myocardial infarction or cardiac arrest)	
Stabile E. (2010)**(109)** Single Centre – Mercogliano, Italy.	CAS	1300 CAS patients (only those that used PEO for neuroprotection): 71.2% Asymptomatic; Mean Age 71.5 years; 69.9% Male	July 2004 to May 2009	30 days from procedure	Symptomatic patients (>= 50% stenosis) and asymptomatic patients (>= 80% stenosis) – NASCET	Symptomatic is defined as carotid stenosis associated, within 6 months before the procedure, with amaurosis fugax, ipsilateral hemispheric TIA, or ipsilateral ischemic stroke not resulting in a major residual neurological deficit Not reported	Procedural: Stroke/Death	By an independent neurologist
Stabile E. (2012)**(110)**	CAS	1611 CAS patients:	Jan 2007 – Dec 2007	30 days from procedure	Symptomatic patients (>=50%) and asymptomatic patients (>=80%; life	Symptomatic - those with ipsilateral amaurosis fugax, ipsilateral hemispheric TIA(s), or ipsilateral ischemic stroke	Procedural: Stroke/Death	Patients assessed after one month with a clinical examination and questionnaire.

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
8 Institutions; Mercogliano, Italy London, Canada Cotignola, Italy Dendermonde, Belgium Mirano, Italy, Sienna, Italy Perugia, Italy Leipzig, Germany Frankfurt, Germany		68.6% Male; 72.6% Asymptomatic; Mean Age: 72.1			expectancy > 5 years) according to NASCET criteria	without major disability (Rankin >3) within 6 months before intervention. Not reported		An independent neurologist, a cardiologist, and a vascular surgeon reviewed all charts as a part of the auditing process
Stromberg S. (2012)**(111)** Swedvasc	CEA	2596 CEA patients: 0% Aymptomatic; Mean Age 71.9 years; 66.7% Male	May 2008 – May 2011	30 days from procedure	Symptomatic patients only selected; degree of stenosis not stated	TIA, minor stroke (symptoms restituted within 1 week or remaining minor dysfunction), or major stroke (disabling stroke) 180 days prior to procedure Procedural stroke/death risks were reported by time for symptom to procedure (0.-2 days:	Procedural: Death, Stroke, Major Stroke, Minor Stroke, Stroke/Death,	Not reported

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
						11.5%; 3-7 days: 3.6%; 8-14 days: 4%; 15-180 days: 5.4%) 40.1% TIA, 35.3% minor stroke, 3% major stroke, 19.6% Amaurosis fugax, 2.1% Crescendo TIA		
Tu J. (2003)**(112)** All CEA's in Ontario Canada – 34 hospitals	CEA	6038 CEAs: 65.3% Male; 30.6% Asymptomatic; Mean Age: 68.3	Jan 1994 – Dec 1997	30 days from procedure.	Symptomatic (87% >= 70%) and asymptomatic patients (97% >= 60%) – states *"Most variable definitions were the same as those used in NASCET"*	Patients were considered symptomatic if they had a history of stroke, TIA, or amaurosis fugax within 6 months of surgery. 77.1% TIA or Stroke; 22.8% Amaurosis fugax	Procedural: Death, Non-fatal Stroke, Stroke/Death	Record linkage
UK CEA audit – round 5**(113, 114)**	CEA	16774 CEAs: 67% Male; Mean Age: 72 Data reported for 2150 Asymptomatic patients only	2011-2013	30 days from procedure.	Symptomatic and Asymptomatic; degree of stenosis not stated Data reported for 2150 Asymptomatic patients only	Symptomatic – History of stroke or TIA Not reported	Procedural: Death, Stroke, Stroke/Death, MI	Post-hospital discharge follow-up assessment

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Vikatmaa P. (2012)**(115)** VASCUNET - Australia, Denmark, Hungary, Italy, Finland, Norway, Sweden, Switzerland and the United Kingdom	CEA	53077 CEAs: 39.9% Asymptomatic Australia (no 30 day outcomes): 33.1% Asymptomatic; Mean Age: 72.4; 70.6% Male Denmark: 0% Asymptomatic; Mean Age: 67.9; 67.7% Male Finland: 15.6% Asymptomatic; Mean Age: 68.4; 68.6% Male Hungary: 46.1% Asymptomatic; Mean Age: 65.9; 61% Male Italy: 68.6% Asymptomatic; Mean Age: 72.2; 68.2% Male Norway: 20.5% Asymptomatic; Mean Age: 68.2; 66.9% Male Sweden: 22.8% Asymptomatic; Mean Age: 70.7; 68% Male	2005-09 + UK for 2010	30 days from procedure	Symptomatic and Asymptomatic; degree of stenosis not stated	Not reported	Procedural: Stroke/Death	Not reported

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
		Switzerland: 40.4% Asymptomatic; Mean Age: 70.6; 71.2% Male UK: 16.8% Asymptomatic; Mean Age: 72.7; 68.9% Male						
Wholey M. (2003)**(116)** 53 participating centres in Europe, South & North America, & Asia – Global CAS Registry	CAS	12392 CASs (11243 patients): 6392 Symptomatic, 4581 Asymptomatic.	June 1997 – Sept 2002	30 days from procedure.	Symptomatic and asymptomatic patients; degree not specified	Not reported	Procedural: Death (Procedure related), Stroke, Stroke/Death, Minor Stroke, Major Stroke	Not reported
Wu T. (2015)**(117)** National Surgical Quality Improvement Program (NSQIP)	CEA	24211 CEAs: 58% male, 100% asymptomatic, Mean Age: 65 years	2005 - 2012	30 days from procedure	Asymptomatic; degree of stenosis not stated	Symptomatic – with a previous diagnosis of TIA, stroke, and stroke without neurologic deficit Not reported	Procedural: Stroke/Death	Not reported

Study and setting	Procedure	Participant characteristics	Recruitment period	Duration of follow-up	Carotid Stenosis characteristics	Symptomatic Definition Type of symptom	Outcomes reported	Method of outcome assessment
Yang (2014)**(118)** Single Institution - Seol, Korea	CEA CAS	CEA: 698 CEAs; 253 Symptomatic;87.5% Male CAS: 455 CASs; 234 Symptomatic;85.7% Male;	March1995 - Dec 2012	30 days from procedure	Symptomatic and Asymptomatic; degree of stenosis not stated	Presence of neurological or ocular symptoms within 6 months prior to CEA or CAS was regarded as symptomatic CEA patients: 5.1% Amaurosis fugax, 44.6% TIA, 50.2% stroke CAS patients: 5.9% Amaurosis fugax, 31.6% TIA, 62.4% stroke	Procedural: Stroke, Ipsi, Non-Ipsi by Symp status	Not reported
Yoshida S. (2013)**(119)** Single Centre - Department of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Centre and Harvard Medical School	CEA CAS	271 CAS patients: 66.1% Male; 31.4% Symptomatic; 17.3% > 80 years 830 CEA patients: 56.6% Male; 32.9% Symptomatic; 19.8% > 80 years	Jan 2005 – Dec 2010	30 days from procedure	Symptomatic and asymptomatic; degree of stenosis not stated	Patients with nonspecific symptoms or undocumented symptom status were considered asymptomatic for the purposes of this study	Procedural: Stroke, Death	Not reported

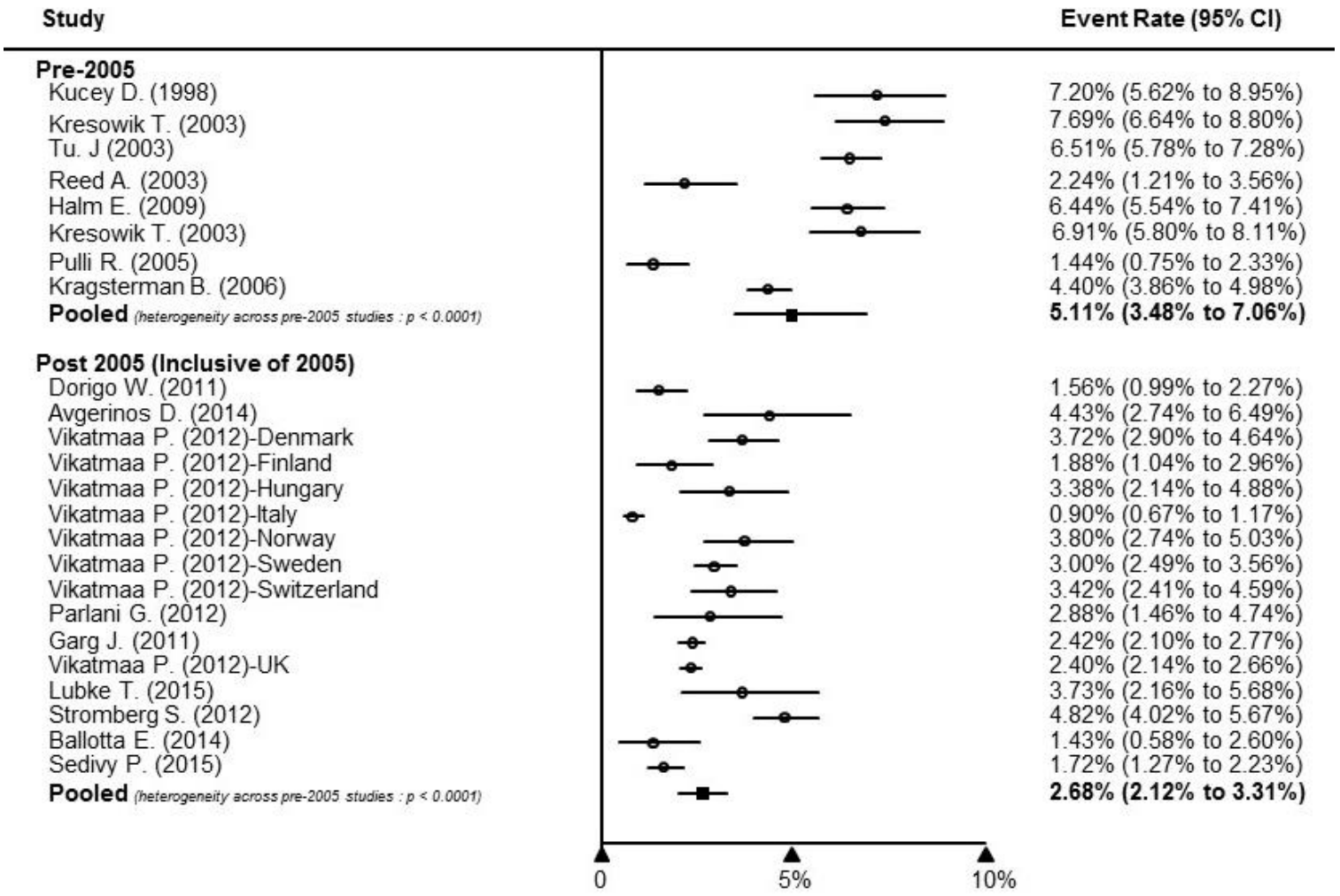
CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; CI: Confidence Interval;

Appendix Table 4.4: Quality assessment scores of included studies

Reference/Study	Adapted single arm Newcastle-Ottawa Quality assessment scale							Total Score
	S1	S2	S3	S4	O1	O2	O3	
Assadian A. (2005)	*	**	*	*		*	*	7
Avgerinos D. (2014)	*	*	*			*	*	5
Ballotta E. (2014)	*	**	*		*	*	*	7
Bekelis K. (2013)	*	*	*	*	*	*	*	7
Bosiers M. (2005)	*	**	*		*	*		6
Bosiers M. (2007)	*	*	*		*	*	*	6
Calvillo-King L. (2010)	*	*	*	*	*	*	*	7
Chaturvedi S. (2010)	*	**	*	*	*	*	*	8
Cremonesi A. (2009)	*	**	*	*		*	*	7
De Rango P. (2011)	*	*	*	*	*	*	*	7
Dorigo W. (2011)		*	*	*	*	*	*	6
Dzierwa K. (2013)	*	*	*	*	*	*	*	7
Egashira Y. (2014)		*	*	*		*	*	5
Garg J. (2011)	*	*	*	*	*	*	*	7
Go C. (2015)	*	*	*			*	*	5
Goode S. (2013)		**	*			*	*	5
Gray A. (2007)	*	**	*		*	*	*	7
Gray W. (2009) – CAPTURE 2	*	**	*	*	*	*	*	8
Gray W. (2009) - EXACT	*	**	*	*	*	*	*	8
Halm E. (2009)	*	*	*	*	*	*	*	7
Hamdan A. (1999)	*	**	*	*		*	*	7
Hopkins L. (2014)	*	**	*		*	*		6
Jalbert J. (2015)		**	*	*	*	*	*	7
Jeffery J. (2014)		**	*	*		*	*	6
Kragsterman B. (2006)	*	*	*	*		*	*	6
Kresowik T. (2014)		*	*		*	*	*	5
Kucey D. (1998)	*	**	*	*	*	*	*	8
Lindstrom D. (2012)	*	*	*	*		*	*	7
Long W. (2007)	*	*	*	*		*	*	6
Lübke T. (2015)	*	**	*		*	*	*	7
Lutz. H (2008)	*	**	*	*	*	*	*	8
Massop D. (2009)	*	*	*	*	*	*	*	7
Mattos A. (2001)	*	**	*			*	*	6
Palombo D. (2009)	*	*	*	*	*	*	*	7
Parlani (2012)	*	*	*	*	*	*	*	7
Pulli R. (2005)	*	**	*	*		*	*	7
Reed A. (2003)	*	**	*			*	*	6
Rockman C. (2005)	*	**	*		*	*	*	7
Rockman C. (2006)	*	*	*	*		*	*	6

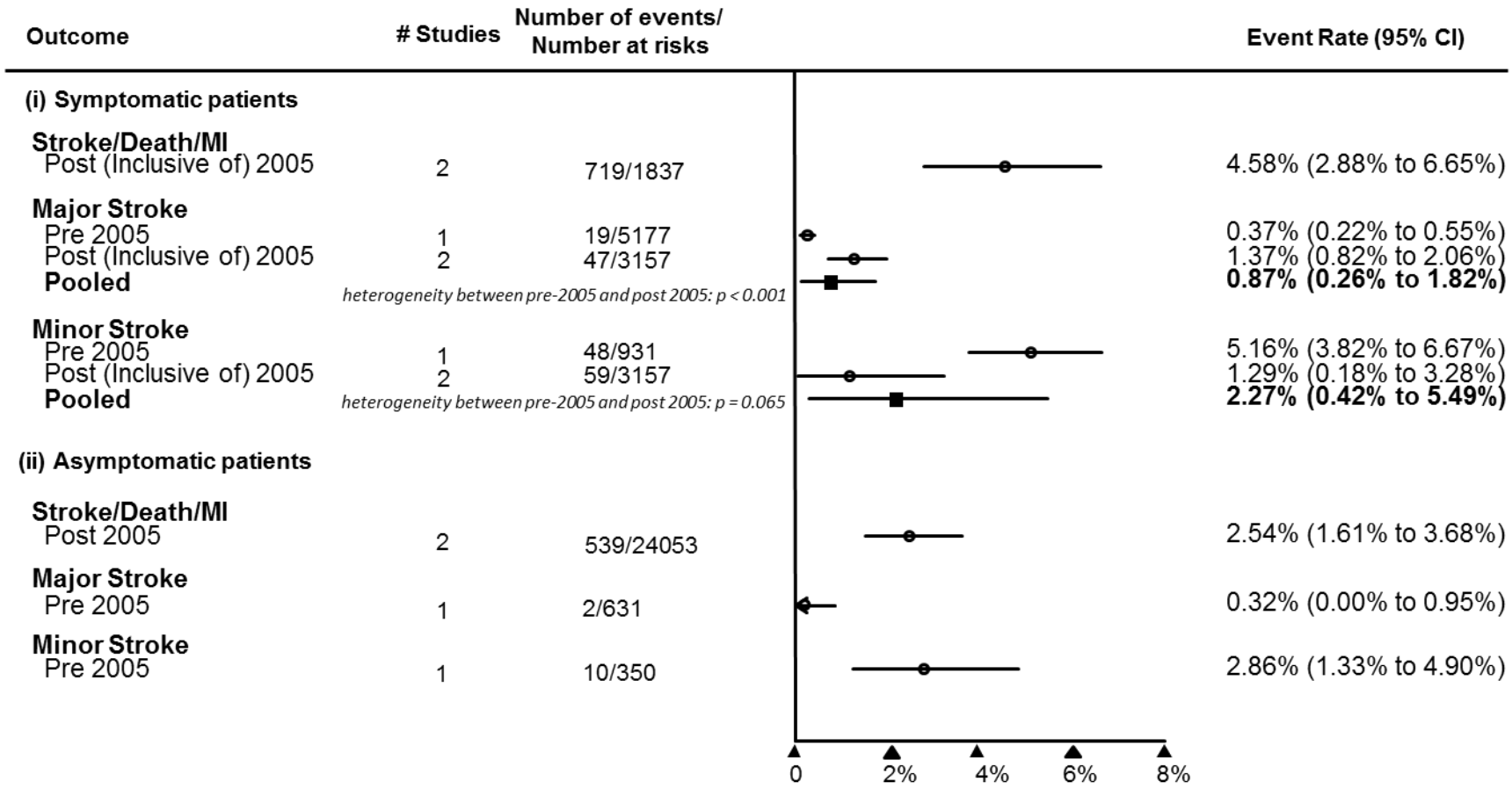
Reference/Study	Adapted single arm Newcastle-Ottawa Quality assessment scale							Total Score
	S1	S2	S3	S4	O1	O2	O3	
Schreiber T. (2010)	*	**	*		*	*	*	7
Šedivý P. (2015)	*	*	*			*	*	5
Setacci C. (2010)		*	*		*	*	*	5
Sidawy A. (2008)	*	*	*	*	*	*	*	7
Stabile E. (2010)		**	*	*	*	*	*	7
Stabile E. (2012)	*	*	*	*	*	*	*	7
Stromberg S. (2012)	*	*	*	*		*	*	6
Tu J. (2003)	*	**	*	*	*	*	*	8
UK CEA audit – round 5	*	*	*	*	*	*	*	7
Vikatmaa P. (2012)	*	**	*			*	*	6
Wholey M. (2003)	*	*	*			*		4
Wu T. (2015)	*	**	*	*		*	*	7
Yang (2014)	*	**	*	*	*	*	*	7
Yoshida S. (2013)	*	**	*	*			*	5

Appendix Figure 4.1: CEA procedural stroke/death rates in symptomatic patients, by study



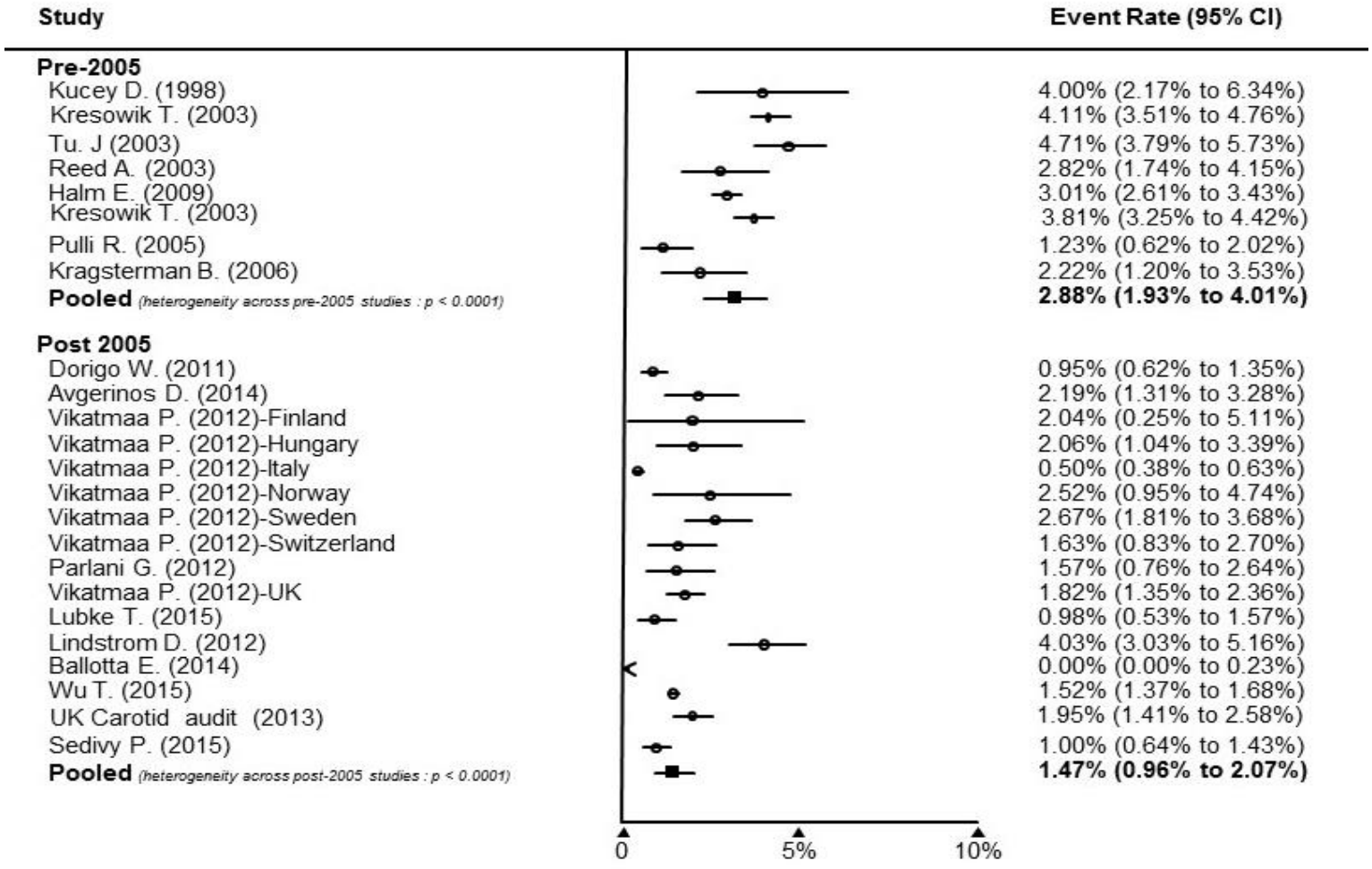
Note: Studies ordered by end of study recruitment year.

Appendix Figure 4.2: Other procedural outcomes of CEA



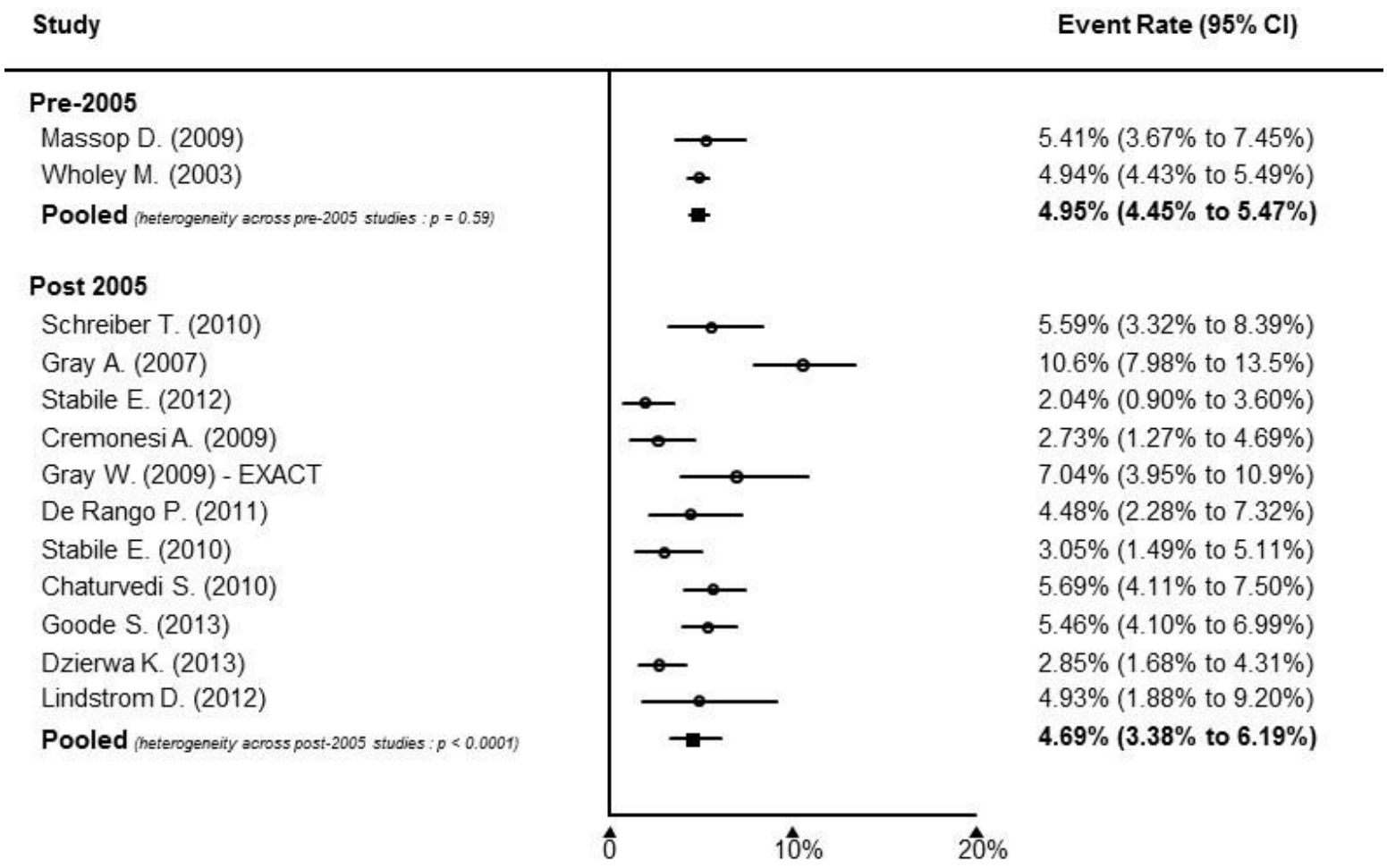
CEA, coronary endarterectomy; MI, myocardial infarction.
Minor stroke defined as modified Rankin Scale (mRS) <3; Major stroke defined as mRS >=3.

Appendix Figure 4.3: CEA procedural stroke/death rates in asymptomatic patients, by study



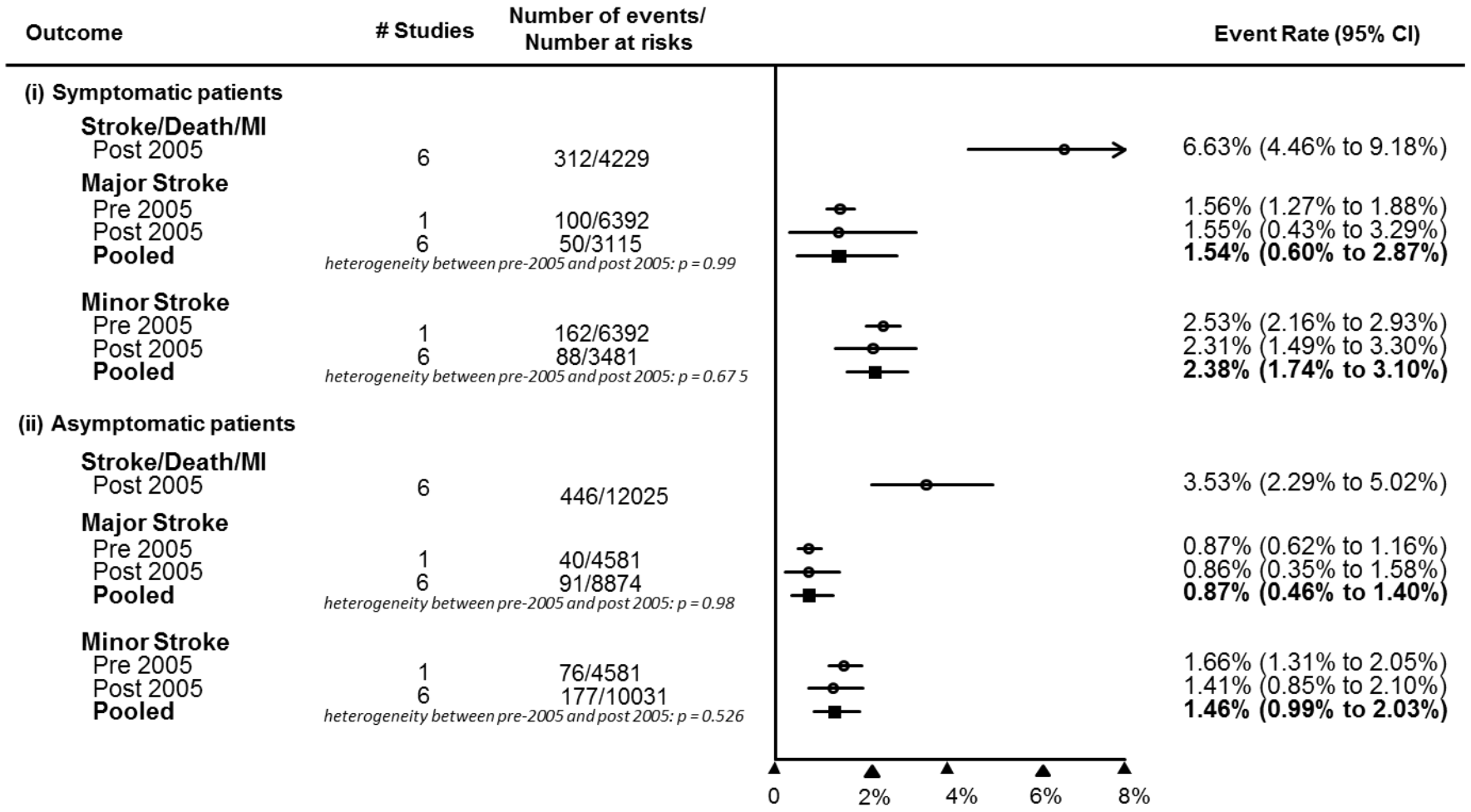
Note: Studies ordered by the end of recruitment year.

Appendix Figure 4.4: CAS procedural stroke/death rates in symptomatic patients, by study



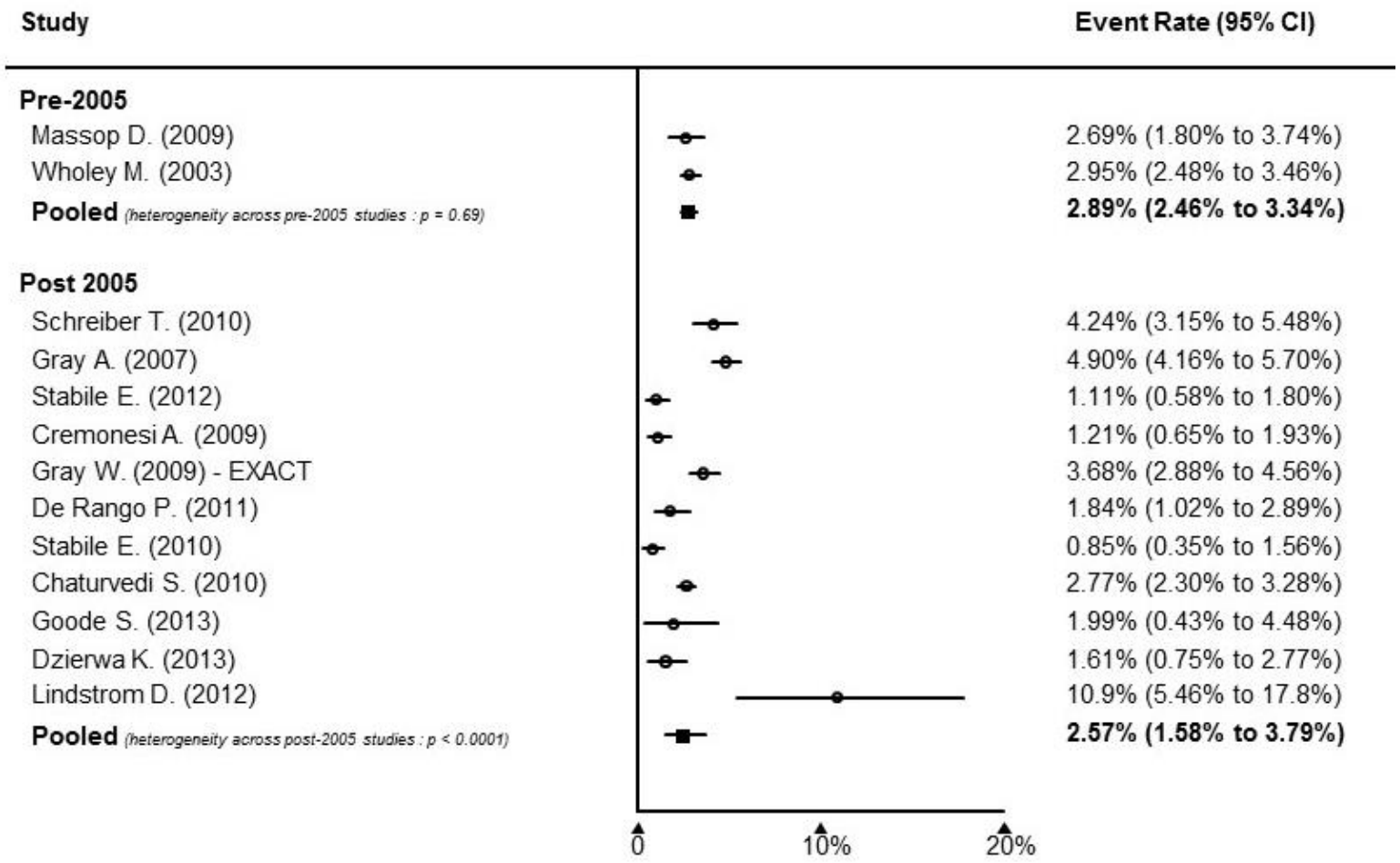
Note: Studies ordered by end of study recruitment year.

Appendix Figure 4.5: Other procedural outcomes of CAS



CAS, carotid artery stenting; MI, myocardial infarction.
Minor stroke defined as modified Rankin Scale (mRS) <3; Major stroke defined as mRS ≥3.

Appendix Figure 4.6: CAS procedural stroke/death rates in asymptomatic patients, by study



Note: Studies ordered by year recruitment completed in study.

Appendix Table 4.5: Meta-analysis of procedural Stroke/Death rates restricted to studies with quality score ≥6

Procedure	Patient Symptomatic Status	End of Study period	# Studies	Events	No. at risk	Procedural Stroke/Death Rate (95% CI)	Heterogeneity p-value[1]
CEA	Symptomatic	Pre-2005	6	766	14485	4.46% (2.65%, 6.70%)	0.031
		Post-2005	13	928	39290	2.52% (1.97%, 3.13%)	
CEA	Asymptomatic	Pre-2005	6	348	11203	2.88% (1.93%, 4.01%)	0.021
		Post-2005	14	689	51772	1.50% (0.96%, 2.15%)	
CAS	Symptomatic	Pre-2005	1	30	555	5.41% (3.67%, 7.45%)	0.524
		Post-2005	10	192	3947	4.61% (3.18%, 6.28%)	
CAS	Asymptomatic	Pre-2005	1	29	1079	2.69% (1.80%, 3.74%)	0.952
		Post-2005	10	459	15246	2.64% (1.54%, 4.00%)	

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; CI: Confidence Interval

[1]p-values from t-tests for differences of procedural stroke/death risks between pre- and post-2005 studies.

Appendix Table 4.6: Procedural stroke/death rates of CEA and CAS in studies classified by method of outcome assessment

Procedure	Patient Symptomatic Status	Method of outcome assessment	End of Study recruitment	Number of Studies	Number Procedural Stroke/Death events	Number of patients	Procedural Stroke/Death Rate (95% CI)	Heterogeneity p-values:		
								between pre-and post-2005	Pre-2005: between studies assessed by independent neurologist or not	Post-2005: between studies assessed by independent neurologist or not
CEA	Symptomatic	By independent neurologist	Pre-2005	0				N/A	N/A	0.695
			Post-2005	2	35	1886	2.04% (0.93%, 3.54%)			
		Not by an independent neurologist	Pre-2005	2	444	6847	6.48% (5.91%, 7.08%)	<0.001		
			Post-2005	3	221	9120	2.40% (1.44%. 3.58%)			
			All Studies	5	665	15967	3.89% (2.10%, 6.21%)			
CEA	Asymptomatic	By independent neurologist	Pre-2005	0				N/A	N/A	0.806
			Post-2005	2	38	3535	1.14% (0.61%, 1.82%)			
		Not by an independent neurologist	Pre-2005	4	603	16483	3.83% (3.16%, 4.56%)	0.27		
			Post-2005	3	33	3738	0.80% (0.01%, 2.59%)			
			All Studies	7	636	20221	2.32% (1.03%, 4.10%)			
CAS	Symptomatic		Pre-2005	1	30	555	5.41% (3.67%, 7.45%)	0.737	N/A	0.309

		By independent neurologist	Post-2005	7	163	3171	4.91% (2.99%, 7.25%)			
			All Studies	8	193	3726	4.96% (3.27%, 6.98%)			
		Not by an independent neurologist	Pre-2005	0				N/A		
			Post-2005	2	22	634	3.45% (1.93%, 5.37%)			
CAS	Asymptomatic	By independent neurologist	Pre-2005	1	29	1079	2.69% (1.80%, 3.74%)	0.879	N/A	0.087
			Post-2005	7	419	13173	2.57% (1.51%, 3.89%)			
			All Studies	8	448	14252	2.59% (1.65%, 3.72%)			
		Not by an independent neurologist	Pre-2005	0				N/A		
			Post-2005	2	29	1972	1.47% (0.91%, 2.15%)			

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; CI: Confidence Interval; N/A: Not applicable

Appendix Table 4.7: Procedural Stroke/Death risks of CEA and CAS separately in studies conducted in North America and Europe

Procedure	Patient Symptomatic Status	Study region	End of Study recruitment	Number of Studies	Number Procedural Stroke/Death events	Number of patients	Procedural Stroke/Death rate (95% CI)	Heterogeneity p-values		
								between pre-and post-2005	Pre-2005: between North America and Europe	Post- 2005: between North America and Europe
CEA	Symptomatic	North America	Pre-2005	6	833	12597	6.09% (4.52%, 7.86%)	0.072	0.198	0.576
			Post-2005	2	217	8577	3.19% (1.50%, 5.48%)			
			All	8	1050	21174	5.30% (3.80%, 7.04%)			
		Europe	Pre-2005	2	241	6081	2.78% (0.62%, 6.37%)	0.924		
			Post-2005	14	906	36639	2.62% (2.02%, 3.30%)			
			All	16	1147	42720	2.65% (2.07%, 3.30%)			
CEA	Asymptomatic	North America	Pre-2005	6	638	17577	3.70% (3.13%, 4.32%)	<0.001	0.013	0.595
			Post-2005	2	387	25079	1.70% (1.13%, 2.38%)			
			All	8	1025	42656	3.15% (2.37%, 4.03%)			
		Europe	Pre-2005	2	26	1610	1.64% (0.80%, 2.76%)	0.762		
			Post-2005	14	346	30068	1.46% (0.92%, 2.11%)			
			All	16	372	31678	1.48% (0.99%, 2.05%)			
CAS	Symptomatic	North America	Pre-2005	1	30	555	5.41% (3.67%, 7.45%)	0.267	N/A	<0.001

			Post-2005	5	125	1738	7.12% (4.95%, 9.63%)			
			All	6	155	2293	6.72% (4.95%, 8.73%)			
		Europe	Pre-2005	0				N/A		
			Post-2005	7	119	3162	3.49% (2.53%, 4.60%)			
CAS	Asymptomatic	North America	Pre-2005	1	29	1079	2.69% (1.80%, 3.74%)	0.12	N/A	0.076
			Post-2005	4	388	10443	3.83% (2.92%, 4.85%)			
			All	5	417	11522	3.61% (2.81%, 4.51%)			
		Europe	Pre-2005	0				N/A		
			Post-2005	7	75	5004	1.89% (0.77%, 3.45%)			

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; CI: Confidence Interval; N/A: Not applicable

Adverse event rates summarised separately for studies completing recruitment before year 2005 ("Pre-2005") or thereafter ("Post-2005"). North America: 12 USA, 3 Canada; Europe: 9 Italy, 5 Sweden, 3 UK, 2 Germany, 1 Belgium, 1 Czech Republic, 1 Poland, 1 Denmark, 1 Finland, 1 Hungary, 1 Norway, 1 Switzerland

Appendix material for Chapter 5

Cost-effectiveness of treatments methods for carotid stenosis in symptomatic and asymptomatic patients

Appendix Text 5.1: Separation of procedural stroke/death risks by stroke severity and mortality

Since information on procedural risks for CEA patients, separately by stroke severity and mortality was limited as reported in **chapter 4**, other data sources were investigated to split overall procedural stroke/death risk into death, non-fatal major, or minor strokes. Proportions of fatalities, procedural major strokes, and procedural minor strokes in procedural stroke/death events from EVA-3S, ICSS, SPACE, CREST and ACT-1 were calculated and synthesized using restricted maximum likelihood random effects meta-analysis methods(120) with Freeman-Tukey (double arcsine) transformation(121, 122) to obtain estimates of proportions of procedural major and procedural minor strokes, separately in procedural stroke/death events. Results from RCTs with both symptomatic and asymptomatic patients were synthesized collectively when calculating these proportions, as no significant differences were observed when proportions were calculated separately for symptomatic and asymptomatic patients. Proportions of procedural major and, separately, procedural minor strokes in procedural stroke/death events in individual RCTs are shown in **appendix table 5.3**.

Appendix Text 5.2: Relative procedural risks of CAS vs CEA

Results from all RCTs were used to calculate relative risks for procedural events except for the endpoint of MI where the SPACE trial did not report procedural MIs and, therefore, did not contribute. Pooled relative risks from RCTs with both symptomatic and asymptomatic patients were used as the relative risks were similar by symptomatic status. When compared to procedural stroke/death risks of CAS in post-2005 observational studies (**chapter 4**), the procedural stroke/death risks estimated using relative risks from RCTs and rates of procedural risks of CEA from post 2005 observational studies, were slightly lower (Symptomatic patients: 4.44% vs 4.69%; Asymptomatic patients: 2.48% vs 2.65%), though not statistically significantly different.

Appendix Text 5.3: Impact of statin therapy on post-procedural stroke risks

The ACST-1 study showed a substantial increase in the use of statins by patients with carotid stenosis from 10% at beginning of the trial in 1993 to more than 80% at the end of trial in 2007(123). The SPARCL trial reported that atorvastatin reduced recurrent stroke risk in patients with history of TIA or stroke and significant carotid stenosis.(124) Thus, to account for the impact statin use has on long-term stroke risks in patients with carotid stenosis, annual post-procedural major and minor stroke rates for asymptomatic CEA plus MT patients were obtained from combining data from ACAS, VA, and ACST-1 trials on patients who were prescribed statins at recruitment and underwent CEA procedure (**table 2**). The annual post-procedural major and minor stroke rates of symptomatic CEA patients were informed by the ICSS trial where 81% of patients randomized to CEA were using statin therapy. (125)

Appendix Text 5.4: Covariance matrix of relative risks of post-procedural major and minor strokes between CEA, CAS and MT

Relative risks of post-procedural major and post-procedural minor strokes with CEA vs MT and with CAS vs CEA were estimated using the network meta-analysis (NMA) reported in **chapter 3.** This meta-analysis also estimated the variance-covariance matrix of relative post-procedural major and minor stroke risks of CEA vs MT, CAS vs CEA, and CAS vs MT, which was used to calculate the Cholesky decomposition matrix; termed matrix $\boldsymbol{T}$ where $\boldsymbol{T}$ multiplied by its transposed matrix gives the covariance matrix of CEA vs MT, CAS vs CEA and CAS vs MT. Sample parameter values (in the form of a vector $\boldsymbol{x}$**)** for relative procedural major and minor stroke risks of CEA vs MT and CAS vs CEA, used in the Monte Carlo simulation described below, was simulated using the equation:

$$\boldsymbol{x} = \boldsymbol{y} + \boldsymbol{T}\boldsymbol{z}$$

where $\boldsymbol{y}$ is a vector of mean values for relative post-procedural major and minor stroke risks for CEA vs MT, CAS vs CEA and CAS vs MT as obtained from the NMA, $\boldsymbol{z}$ is a vector of independent variable with a standard normal distribution. This was used to generate random variables for the Monte Carlo simulation described below which informed the probabilistic sensitivity analysis.

Appendix Text 5.5: Increased non-stroke vascular mortality risks in stroke patients

Results from ECST showed that in patients with a purely unilateral arterial disease the 5-year non-stroke vascular mortality risk was 2.7%, resulting in a per annum rate of 0.54%. Given that non-stroke vascular mortality risks in the general UK population aged 65 to 69 was 0.22%, it was assumed that patients in the model who had experienced a stroke had 2.45 times increased non-stroke vascular mortality risk.

Appendix Text 5.6: QoL of asymptomatic patients – control patients' sample in OxVasc

At each OxVasc follow-up point, cases (stroke or TIA survivors from the OxVasc population) were matched 1:1 with controls from the 2006 Health Survey for England (HSE) survey. Controls were obtained by matching cases with those in the 2006 HSE survey by age at time of follow-up (categorized as younger/older than 70 years); sex; history of diabetes, angina/myocardial infarction, stroke, hypertension, and disability; and marital status. When more than one control was identified, preference was given to controls with the closest age and education levels. The QoL for these patients was reported to be 0.85 (Standard Error (SE): 0.011).(126) Health related QoL in OxVasc was measured using the eq-5d 3 level questionnaire where patients were required to report problems in 5 attributes, with eq-5d responses converted to utilities using UK population tariffs.(127)

Appendix Text 5.7: Health related QoL at baseline in RCTs

QoL of patients diagnosed with carotid stenosis using a EQ-5D elicitation method was reported by two sources. The ICSS study (symptomatic patients with a mean age of 70 recruited in Europe, Australia, New Zealand, and Canada from 2001-08) reported a QoL of 0.76 (SE: 0.008) for patients randomised to CEA and 0.78 (SE 0.007) for patients randomised to CAS which was similar to that of patients having experiences a minor stroke or TIA in the OxVASC population. SAPPHIRE (30% symptomatic patients, 70% asymptomatic patients with a mean age of 72 years recruited in Europe, Australia and Canada) (128) reported a QoL of 0.72 for patients randomised to CEA and 0.73 for patients randomised to CAS. These were lower than QoL of the age-matched general UK population despite a large proportion of patients being asymptomatic. This is likely due to the inclusion criteria in SAPPHIRE population which required all patients to have at least one coexisting condition that increased the risk for CEA.(129)

Appendix Text 5.8: QoL of patients after CEA and CAS procedures

Results from the SAPPHIRE trial show no significant differences in QoL of patients between baseline and 2 weeks from procedure for both CEA and CAS, indicating that neither procedure has an impact on QoL.(128) Results from CREST(130) showed that there was a significant differences in the QoL, as estimated by the physical component summary scale[2] on the SF-36 scale, of CEA patients at 2 weeks and 1 months follow-up when compared to CAS patients, but these differences had resolved at 1-year. Given that no differences were observed between baseline and 1-year post procedure and in view of lack of data on differences in QoL utilities; it was assumed that undergoing CEA or CAS was not associated with a change in QoL.

[2] SF-36 provides summary scales for overall physical and mental health.

No QoL data were reported immediately after procedure in ICSS.(131) Thus there was no evidence from the ICSS trial that showed a change in QoL after CEA or CAS procedure.

Appendix Text 5.9: QoL after stroke

When considering all strokes, patients in OxVasc had a QoL of 0.70 (0.13) one-year after stroke showing a 0.15 decrease in QoL. QoL estimates did not differ significantly at 2 years (0.66 (0.018)) and 5 years (0.68 (0.019)) follow-up. Other studies looking at the effect of stroke on QoL show similar results with a 0.17 (0.035) permanent decrement in QoL of patients with diabetes(132) in one study, and a 0.14 (0.041) decrement in QoL of patients with a history of cardiovascular disease, during the annual periods with stroke event and 0.12 (0.021) decrement in subsequent years of follow-up in another study.(133) Health related QoL after stroke in OxVasc was measured using the eq-5d 3 level questionnaire where patients were required to report problems in 5 attributes, with eq-5d responses converted to utilities using UK population tariffs.(127)

Appendix Text 5.10: Post major and minor stroke costs in OxVasc

In the OxVasc study, resource use was obtained from patient hospital records from the date of first TIA or stroke, to up to 5 years follow-up or death. Resource use was obtained from patients' hospital records from the index event until March 31st 2010, with a minimum follow-up of 5 years. Patient hospital records from the Oxford Radcliffe Hospitals National Health Service Trust (1 tertiary hospital, 3 acute general hospitals, and 9 community hospitals) were reviewed for any accident and emergency visit, emergency transport, outpatient care visit, day case, or hospitalization. Patients were followed up by a research nurse and general practitioner with admissions to nursing or residential care homes also recorded. Long-term hospitalizations during which patients were admitted and discharged on the same day were classified as day cases and the number of days in hospital was set to 0. Unit costs for day case of days in hospital for each hospital

ward were obtained from the schedule of reference costs for the NHS and NHS trust financial returns, with the exception of the cost per day in a stroke unit which was obtained from a previously published report on costs of secondary care in the OxVasc study for patients recruited from 2002-04. (134) Unit costs for outpatient, accident and emergency visits were obtained from the schedule of NHS reference costs. While it was difficult to separate between acute care and rehabilitation care in the UK, rehabilitation in the UK generally starts in the stroke unit or general ward with some patients either being admitted for several weeks for rehabilitation or transferred to specialist rehabilitation wards in community hospitals. Strokes were classified by stroke severity according to the National Institutes of Health Stroke Scale (NIHSS), with minor strokes defined as NIHSS $\leq$3, and major stroke as NIHSS > 3.

Appendix Text 5.11: 2014-15 HRG National Schedule for Reference cost of CEA and CAS

In the sensitivity analysis, the cost of CEA and CAS was sourced from the 2014-15 HRG National Schedule for Reference cost. (135) The cost of CEA (£4597) was calculated by taking a weighted average by finished consultant episodes of HRG currency codes YQ31A and YQ31B which were obtained by matching OPCS codes L291, L293, L294, L295, L298, L299 and L301 using the HRG 2015/16 Reference Costs Grouper Code to Group Workbook. Similarly, the cost of CAS (£6575) was from HRG currency code YA10 which were obtained by matching OPCS codes L311, L313, and L314. Costs of both elective and non-elective procedures were included in the calculations. A breakdown of the calculations and descriptions of HRG currency codes used are shown in **appendix table A5.5**, and descriptions of the OPCS codes used are given in **appendix table A5.6**.

Appendix Text 5.122: AdVISHE checklist(136)

A1: Face validity testing (conceptual model): Have experts been asked to judge the appropriateness of the conceptual model?

Yes. Two of my supervisors, Prof. Alison Halliday and Dr. Richard Bulbulia who are clinicians working with the ACST-2 RCT comparing interventions for carotid stenosis, and involved with the Carotid Stenosis Trialists' Collaboration (CSTC) group gave inputs when developing the conceptual framework and gave the go ahead with regard to the underlying clinical process and disease stages.

A2: Cross validity testing (conceptual model): Has this model been compared to other conceptual models found in the literature or clinical textbooks?

Yes, the model has been compared to other decision analytical models identified in **chapter 2** (**table 2.1**)

B1: Face validity testing (input data): Have experts been asked to judge the appropriateness of the input data?

Yes, Prof. Alison Halliday and Dr. Richard Bulbulia who are clinicians working with the ACST-2 RCT comparing interventions for carotid stenosis, and involved with the Carotid Stenosis Trialists' Collaboration (CSTC), looked at the appropriateness of the model input parameters.

B2: Model fit testing: When input parameters are based on regression models, have statistical tests been performed?

Main model input parameters for clinical parameters were based on information from RCTs, results from meta-analyses in chapters 3 and 4 where test for heterogeneity was performed, and information from the mortality statistics in the UK. Cost of CEA and CAS were obtained from recourse use information in ICSS, and MT from the British National formulary. Hence these parameters were not based on regression models. In costs of stroke, obtained from OxVasc, validity of regression models performed were assessed by looking at whether residuals were normally distributed, and whether there were patterns in residuals when plotted against predicted values. For HrQoL, obtained from OxVasc, regression techniques were used when converting eq-5d responses to utilities.

C1: External review: Has the computerized model been examined by modelling experts

Yes, the computerized model was examined by my primary supervisor, Prof. Borislava Mihaylova who is an experienced Health Economist.

C2: Extreme value testing: Has the model been run for specific, extreme sets of parameter values in order to detect any coding errors?

The model has been run by setting both procedural costs of CEA and CAS to zero (**appendix table 5.22),** and by setting the treatment effects between treatment methods to one (**appendix table 5.23**).

C3: Testing of traces: Have patients been tracked through the model to determine whether its logic is correct?

The number of patients in each disease state was listed at each annual Markov cycle. The patients in all disease states were added up at each time point to check if it was equal to 1000 (1000 being the number of patients in the cohort).

C4: Unit testing: Have individual sub-modules of the computerized model been tested?

All macros written in VBA were re-examined to check if error free. Validity of macro generated results across various sub-group patient categories were also tested for validity (eg: comparisions of predicted life years between symptomatic and asymptomatic patients, and between younger and older patients, comparison of predicted QALYs against predicted life years, comparison of intersection points in macro generated cost-effectiveness acceptability curves with ICERs).

D1: Face validity testing (model outcomes): Have experts been asked to judge the appropriateness of the model outcomes?

The appropriateness of the model outcomes were judged by both my clinical supervisors Prof. Alison Halliday and Dr. Richard Bulbulia, and by my two other supervisors Prof. Borislava Mihaylova and Prof. Alastair Gray who are 2 experienced Health Economists. All supervisors concluded that the model outcome were reasonable.

D2: Cross validation testing (model outcomes): Have the model outcomes been compared to the outcomes of other models that address similar problems?

The model outcomes were compared to a previous economic evaluations by Morris et al, (23) and Thapar et al(17), with reasons behind differences pointed in in pages 171-173 in the main thesis, and in **appendix text 5.13**.

D3: Validation against outcomes using alternative input data: Have the model outcomes been compared to the outcomes obtained when using alternative input data?

Model was adjusted to a 5-year time horizon, and model inputs for relative post-procedural stroke risks were sourced from the ICSS trial alone in attempt to replicate results of symptomatic patients to that of Morris et al(23) with results presented in **appendix table 5.21.**

D4: Validation against empirical data: Have the model outcomes been compared to empirical data?

Life expectancy of patients in each treatment arm were compared to life expectancy of patients in general UK population, with results presented in **figure 5.14 – 5.15**.

E1: Other validation techniques: Have any other validation techniques been performed?

No other model validation techniques were performed

Appendix Text 5.13: Reasons behind difference in results when compared to Morris et al

The differences in results were driven by a combination of factors. Firstly, post-procedural major and minor stroke relative risks between CEA+MT and CAS+MT in Morris et al(23) were informed by a single RCT; ICSS, while the economic evaluation in this chapter takes into account all available evidence from RCTs. This included information from CREST in addition to ICSS, with CREST showing results more supportive of CEA+MT than CAS+MT with regard to post-procedural major stroke risks. Secondly Morris et al(23) was limited to a 5-year time horizon resulting in the long-term stroke risk reduction when being treated with CEA+MT when compared to CAS+MT as shown in RCTs is not present through the lifetime of the patients. Third, Morris et al(23) used procedural risks of CEA from ICSS where patients were recruited from 2000-08, and are not reflective of contemporary practise, with results from **chapter 4** showing that procedural stroke/death risks of CEA have decreased post-2005 to 2.68% in symptomatic patients when compared to 3.97% in ICSS. Fourth, in Morris et al costs of managing patients who had experienced a stroke post intervention was calculated by combining data from ICSS and OxVasc to derive the costs of managing stroke based on a patient's sex, age, disability before stroke, previous history of cardiovascular disease, stroke severity and recurrent strokes. Fifth, health related QoL of patients in Morris et al was obtained from patients in the ICSS trial on a EQ-5D scale at one, six months and then on an annual basis until 5 years

Appendix Table 5.1: Model input parameters for post-procedural stroke risks by age and gender in asymptomatic patients

Age	Post-procedural major strokes (including fatal strokes) (p.a)						Post-procedural minor strokes (p.a)					
	MT alone*		CEA plus MT		CAS plus MT		MT alone*		CEA plus MT		CAS plus MT	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
65	0.84%	0.66%	0.45%	0.36%	0.55%	0.44%	1.13%	0.89%	0.55%	0.43%	0.69%	0.55%
66	0.87%	0.69%	0.47%	0.37%	0.57%	0.45%	1.17%	0.92%	0.57%	0.45%	0.72%	0.57%
67	0.90%	0.71%	0.48%	0.38%	0.59%	0.47%	1.21%	0.95%	0.59%	0.46%	0.75%	0.59%
68	0.93%	0.73%	0.50%	0.40%	0.61%	0.48%	1.25%	0.99%	0.61%	0.48%	0.77%	0.61%
69	0.96%	0.76%	0.52%	0.41%	0.63%	0.50%	1.29%	1.02%	0.63%	0.50%	0.80%	0.63%
70	0.99%	0.78%	0.53%	0.42%	0.65%	0.51%	1.33%	1.05%	0.65%	0.51%	0.83%	0.65%
71	1.02%	0.81%	0.55%	0.44%	0.67%	0.53%	1.37%	1.09%	0.67%	0.53%	0.84%	0.67%
72	1.05%	0.83%	0.57%	0.45%	0.70%	0.55%	1.42%	1.12%	0.69%	0.55%	0.87%	0.69%
73	1.09%	0.86%	0.59%	0.46%	0.72%	0.57%	1.47%	1.16%	0.71%	0.56%	0.90%	0.71%
74	1.12%	0.89%	0.61%	0.48%	0.74%	0.59%	1.51%	1.20%	0.74%	0.58%	0.93%	0.73%
75 to 95	1.16%	0.92%	0.63%	0.50%	0.77%	0.61%	1.56%	1.24%	0.76%	0.60%	0.96%	0.76%

**In MT alone arm, post-procedural risks refers to all stroke risks since there are no procedural risks involved with MT*

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; p.a: per annum

Appendix Table 5.2: Model input parameters for post-procedural stroke risks by age and gender in symptomatic patients

Age	Post-procedural major strokes (including fatal strokes) (p.a)						Post-procedural minor strokes (p.a)					
	MT alone*		CEA plus MT		CAS plus MT		MT alone*		CEA plus MT		CAS plus MT	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
65	1.92%	1.52%	1.04%	0.82%	1.27%	1.00%	1.01%	0.79%	0.49%	0.39%	0.62%	0.49%
66	1.99%	1.57%	1.07%	0.85%	1.31%	1.04%	1.04%	0.82%	0.51%	0.40%	0.64%	0.51%
67	2.05%	1.62%	1.11%	0.88%	1.35%	1.07%	1.07%	0.85%	0.52%	0.41%	0.66%	0.52%
68	2.12%	1.67%	1.15%	0.91%	1.40%	1.10%	1.11%	0.88%	0.54%	0.43%	0.69%	0.54%
69	2.19%	1.73%	1.18%	0.93%	1.44%	1.14%	1.15%	0.90%	0.56%	0.44%	0.71%	0.56%
70	2.26%	1.79%	1.22%	0.97%	1.49%	1.18%	1.18%	0.93%	0.58%	0.45%	0.73%	0.58%
71	2.33%	1.84%	1.26%	1.00%	1.54%	1.22%	1.22%	0.97%	0.59%	0.47%	0.75%	0.59%
72	2.41%	1.90%	1.30%	1.03%	1.59%	1.26%	1.26%	1.00%	0.61%	0.48%	0.77%	0.61%
73	2.49%	1.97%	1.35%	1.06%	1.64%	1.30%	1.30%	1.03%	0.63%	0.50%	0.80%	0.63%
74	2.57%	2.03%	1.39%	1.10%	1.70%	1.34%	1.35%	1.06%	0.65%	0.52%	0.83%	0.65%
75 to 95	2.66%	2.10%	1.44%	1.14%	1.75%	1.39%	1.39%	1.10%	0.68%	0.53%	0.85%	0.67%

**In MT alone arm, post-procedural risks refers to all stroke risks since there are no procedural risks involved with MT*

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; p.a: per annum

Appendix Table 5.3: Proportion of procedural major and procedural minor strokes in procedural events in randomised controlled trials

Trial	Symptomatic status	Procedural stroke/death (n)	Procedural major strokes*		Procedural minor strokes*	
			n	%[1]	n	%[1]
EVA-3S	Symptomatic	10	3	30.0%	6	60.0%
CREST	Symptomatic	21	6	28.6%	15	71.4%
CREST	Asymptomatic	8	2	25.0%	6	75.0%
SPACE	Symptomatic	39	21	53.8%	16	41.0%
ICSS	Symptomatic	34	21	61.8%	11	32.4%
ACT-1	Asymptomatic	6	1	16.7%	4	66.7%
Overall						

*****Event rates do not add up to one due to procedural fatal MIs not shown; [1]percentage of procedural stroke/deaths*
EVA-3S: Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; CREST: Carotid Revascularization Endarterectomy vs. Stenting Trial; SPACE: Stent-Protected Angioplasty versus Carotid Endarterectomy; ICSS: International Carotid Stenting Study; ACT-1: Asymptomatic Carotid Trial

Appendix Table 5.4: EQ-5D measure of quality of life from HSE 2003, 2006 and 2011

Age group	n	Utility	se
55-59	2768	0.830	0.25
60-64	2427	0.818	0.24
65-69	2015	0.817	0.24
70-74	1641	0.802	0.24
75-79	1252	0.784	0.24
80-84	742	0.749	0.23
85+	370	0.719	0.26

HSE: Health Survey for England; se: standard error; n: number

Appendix Table 5.5: Hospital admission cost for CEA and CAS using UK HRG costs

HRG Code	HRG Description	Finished consultant episodes (FCEs)	Episode Cost (UK £)
	CEA		
YQ31A	Single Open Procedure on Carotid Artery with CC Score 5+	1125	5347
YQ31B	Single Open Procedure on Carotid Artery with CC Score 0-4	2882	4304
CEA episode cost (weighted average of categories of FCEs)			**4597**
	CAS		
YA10Z	Percutaneous Transluminal Angioplasty, including Stenting, of Intracranial or Extracranial Blood Vessel	533	6575
CAS episode cost			**6575**

Data from 2014-15 HRG National Schedule for Reference costs data (135)

HRG: Healthcare Resource Group; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Table 5.6: OPCS codes of CEA and CAS

Code system	Code	Code description
CEA		
OPCS 4	L291	Replacement of carotid artery using graft
OPCS 4	L293	Bypass to carotid artery NEC
OPCS 4	L294	Endarterectomy of carotid artery and patch repair of carotid artery
OPCS 4	L295	Endarterectomy of carotid artery NEC
OPCS 4	L298	Other specified reconstruction of carotid artery
OPCS 4	L299	Unspecified reconstruction of carotid artery
OPCS 4	L301	Repair of carotid artery NEC
CAS		
OPCS 4	L311	Percutaneous transluminal angioplasty of carotid artery
OPCS 4	L313	Endovascular repair of carotid artery
OPCS 4	L314	Percutaneous transluminal insertion of stent into carotid artery

OPCS: Operating Procedure Code; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Table 5.7: List of medical therapies typically used in patients with carotid stenosis

	Unit price (per tablet)	Daily dose	Annual cost (UK £)*	Patent
Antiplatelet				
Aspirin 75mg	0.028	75mg	10	Non-proprietary
Clopidogrel 75mg	0.072	75mg	20	Non-proprietary
Statins				
Atorvastatin 40mg	0.072	2 x 40mg	40	Non-proprietary
Antihypertensive				
Amlodipine 5mg	0.051	2 x 5mg	37	Non-proprietary

Data obtained from the 2017 edition of the British National Formulary(137)

Appendix Table 5.8: Projected per annum stroke risks at 1, 5, 10 and 15 years

Patient group	Time Horizon	MT				CEA + MT				CAS + MT				Total Strokes: MT – CEA+MT	Total Strokes: MT – CAS+MT	Total Strokes: CAS+MT – CEA+MT
		Minor strokes	Non-fatal Major Stroke	Fatal Stroke	Total strokes	Minor strokes	Non-fatal Major Stroke	Fatal Stroke	Total strokes	Minor strokes	Non-fatal Major Stroke	Fatal Stroke	Total strokes			
65 year old Asymptomatic Men	1 year	1.19%	0.60%	0.29%	2.08%	1.43%	0.77%	0.37%	2.56%	2.50%	0.99%	0.47%	3.96%	-0.48%	-1.89%	1.40%
	5 year	1.27%	0.67%	0.32%	2.26%	0.80%	0.45%	0.22%	1.47%	1.16%	0.57%	0.27%	2.00%	0.79%	0.26%	0.54%
	10 years	1.37%	0.76%	0.36%	2.49%	0.77%	0.45%	0.21%	1.43%	1.05%	0.56%	0.27%	1.88%	1.06%	0.61%	0.45%
	15 years	1.43%	0.82%	0.39%	2.64%	0.77%	0.46%	0.22%	1.45%	1.03%	0.57%	0.28%	1.88%	1.19%	0.76%	0.43%
65 year old Asymptomatic Women	1 year	0.94%	0.47%	0.22%	1.64%	1.30%	0.69%	0.33%	2.33%	2.33%	0.90%	0.43%	3.66%	-0.69%	-2.03%	1.34%
	5 year	1.00%	0.52%	0.25%	1.77%	0.66%	0.38%	0.18%	1.22%	0.99%	0.47%	0.23%	1.68%	0.56%	0.09%	0.46%
	10 years	1.08%	0.59%	0.28%	1.95%	0.62%	0.36%	0.17%	1.16%	0.86%	0.45%	0.22%	1.53%	0.80%	0.42%	0.37%
	15 years	1.13%	0.64%	0.30%	2.07%	0.62%	0.37%	0.18%	1.16%	0.84%	0.46%	0.22%	1.51%	0.90%	0.55%	0.35%
75 year old Asymptomatic Men	1 year	1.61%	0.81%	0.39%	2.80%	1.65%	0.89%	0.42%	2.96%	2.80%	1.14%	0.55%	4.49%	-0.16%	-1.69%	1.53%
	5 year	1.61%	0.84%	0.40%	2.86%	0.98%	0.55%	0.26%	1.80%	1.40%	0.69%	0.33%	2.42%	1.06%	0.43%	0.63%
	10 years	1.61%	0.88%	0.42%	2.90%	0.90%	0.52%	0.25%	1.67%	1.24%	0.65%	0.31%	2.20%	1.23%	0.70%	0.53%
	15 years	1.61%	0.89%	0.43%	2.93%	0.88%	0.52%	0.25%	1.65%	1.20%	0.64%	0.31%	2.15%	1.28%	0.77%	0.51%
75 year old Asymptomatic Women	1 year	1.26%	0.63%	0.30%	2.20%	1.47%	0.79%	0.38%	2.64%	2.56%	1.02%	0.49%	4.07%	-0.44%	-1.87%	1.43%
	5 year	1.26%	0.66%	0.31%	2.24%	0.80%	0.45%	0.22%	1.47%	1.17%	0.57%	0.27%	2.01%	0.76%	0.23%	0.53%
	10 years	1.26%	0.68%	0.33%	2.27%	0.72%	0.42%	0.20%	1.34%	1.00%	0.52%	0.25%	1.78%	0.93%	0.49%	0.43%

	15 years	1.26%	0.69%	0.33%	2.29%	0.70%	0.41%	0.20%	1.31%	0.96%	0.51%	0.25%	1.72%	0.98%	0.57%	0.41%
65 year old Symptomatic Men	1 year	1.07%	1.39%	0.66%	3.12%	2.07%	1.55%	0.74%	4.35%	3.91%	2.01%	0.96%	6.88%	-1.23%	-3.76%	2.53%
	5 year	1.14%	1.51%	0.72%	3.37%	0.89%	0.98%	0.47%	2.34%	1.42%	1.24%	0.59%	3.25%	1.02%	0.12%	0.90%
	10 years	1.23%	1.65%	0.79%	3.67%	0.79%	0.98%	0.47%	2.23%	1.16%	1.22%	0.59%	2.97%	1.43%	0.70%	0.74%
	15 years	1.27%	1.74%	0.83%	3.84%	0.77%	1.00%	0.48%	2.24%	1.10%	1.24%	0.60%	2.94%	1.60%	0.90%	0.70%
65 year old Symptomatic Women	1 year	0.84%	1.09%	0.52%	2.45%	1.94%	1.38%	0.66%	3.98%	3.73%	1.80%	0.86%	6.39%	-1.53%	-3.94%	2.41%
	5 year	0.90%	1.18%	0.56%	2.64%	0.76%	0.81%	0.38%	1.95%	1.24%	1.01%	0.49%	2.74%	0.69%	-0.10%	0.79%
	10 years	0.97%	1.29%	0.62%	2.88%	0.65%	0.79%	0.38%	1.81%	0.97%	0.98%	0.47%	2.42%	1.07%	0.46%	0.61%
	15 years	1.01%	1.37%	0.65%	3.02%	0.62%	0.80%	0.38%	1.80%	0.90%	0.99%	0.48%	2.37%	1.22%	0.65%	0.57%
75 year old Symptomatic Men	1 year	1.45%	1.87%	0.89%	4.22%	2.32%	1.83%	0.88%	5.02%	4.28%	2.37%	1.13%	7.78%	-0.81%	-3.57%	2.76%
	5 year	1.45%	1.91%	0.91%	4.27%	1.09%	1.22%	0.58%	2.89%	1.71%	1.53%	0.73%	3.97%	1.38%	0.30%	1.08%
	10 years	1.45%	1.94%	0.93%	4.32%	0.95%	1.16%	0.55%	2.67%	1.43%	1.45%	0.70%	3.58%	1.65%	0.74%	0.91%
	15 years	1.45%	1.96%	0.93%	4.34%	0.93%	1.15%	0.55%	2.63%	1.38%	1.44%	0.69%	3.51%	1.71%	0.83%	0.88%
75 year old Symptomatic Women	1 year	1.13%	1.47%	0.70%	3.30%	2.13%	1.60%	0.76%	4.49%	4.01%	2.08%	0.99%	7.08%	-1.19%	-3.77%	2.58%
	5 year	1.13%	1.49%	0.71%	3.34%	0.91%	0.99%	0.47%	2.37%	1.46%	1.24%	0.59%	3.29%	0.97%	0.05%	0.92%
	10 years	1.13%	1.51%	0.72%	3.37%	0.77%	0.92%	0.44%	2.13%	1.17%	1.15%	0.55%	2.87%	1.24%	0.50%	0.74%
	15 years	1.13%	1.53%	0.73%	3.39%	0.74%	0.91%	0.43%	2.09%	1.10%	1.14%	0.55%	2.78%	1.30%	0.61%	0.70%

**Note: Limited to only first strokes experienced by a patient. No recurrent strokes included in analysis*

MT: Medical Therapy; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting

Appendix Table 5.9: Cost-effectiveness results – Undiscounted life years, QALYs and lifetime costs; Discounted incremental results

Patient Group	MT alone			CEA + MT			CAS + MT			CEA +MT vs MT alone		
	LY[1]	QALY[1]	Cost(£)[1]	LY[1]	QALY[1]	Cost(£)[1]	LY[1]	QALY[1]	Cost(£)[1]	Inc QALYs[2]	Inc Cost(£)[2]	ICER(£)[2]
65 year old Asymptomatic Men	14.84 (14.45,15.13)	12.26 (11.8,12.64)	9290 (6812,12446)	15.19 (12.55,12.86)	12.7 (15.07,15.33)	10752 (9489,11901)	15.06 (14.81,15.29)	12.53 (12.25,12.81)	12458 (10370,14530)	0.26 (0.09,0.5)	2446 (740,3623)	9502 (1684,39173)
65 year old Asymptomatic Women	17.16 (16.79,17.45)	14.15 (13.7,14.5)	9556 (7073,12723)	17.48 (14.39,14.71)	14.55 (17.36,17.6)	11020 (9625,12150)	17.36 (17.11,17.57)	14.39 (14.07,14.66)	12790 (10633,14748)	0.23 (0.07,0.48)	2548 (533,3680)	11047 (1161,51996)
70 year old Asymptomatic Men	11.55 (11.28,11.74)	9.43 (9.11,9.66)	6539 (4996,8672)	11.78 (9.62,9.81)	9.7 (11.7,11.86)	8981 (8102,9716)	11.68 (11.51,11.84)	9.59 (9.4,9.78)	10268 (8794,11660)	0.18 (0.06,0.36)	3017 (1658,3900)	17152 (4803,62082)
70 year old Asymptomatic Women	13.46 (13.21,13.64)	10.97 (10.66,11.18)	6766 (5104,9239)	13.67 (11.14,11.34)	11.22 (13.6,13.76)	9216 (8252,9982)	13.59 (13.41,13.73)	11.11 (10.9,11.29)	10554 (9037,12039)	0.16 (0.04,0.34)	3087 (1729,3949)	19419 (4965,79873)
75 year old Asymptomatic Men	8.51 (8.34,8.66)	6.82 (6.62,6.98)	4700 (3487,6228)	8.67 (6.94,7.07)	7 (8.62,8.73)	7759 (7052,8262)	8.6 (8.49,8.71)	6.92 (6.8,7.05)	8737 (7705,9607)	0.13 (0.04,0.27)	3377 (2171,4124)	26840 (8115,103224)
75 year old Asymptomatic Women	10.01 (9.83,10.14)	8 (7.8,8.16)	4839 (3598,6425)	10.14 (8.11,8.25)	8.17 (10.09,10.21)	7924 (7176,8437)	10.08 (9.96,10.19)	8.09 (7.96,8.22)	8937 (7795,9915)	0.11 (0.03,0.25)	3437 (2234,4151)	30321 (9525,137508)
80 year old Asymptomatic Men	5.96 (5.84,6.04)	4.66 (4.53,4.76)	2948 (2162,3949)	6.03 (4.72,4.79)	4.75 (6.01,6.07)	6633 (6124,7008)	5.99 (5.93,6.06)	4.7 (4.64,4.78)	7339 (6633,7992)	0.07 (0.01,0.16)	3833 (2974,4360)	56735 (18725,264185)
80 year old Asymptomatic Women	7.02 (6.92,7.09)	5.49 (5.37,5.57)	3018 (2267,4005)	7.08 (5.54,5.62)	5.57 (7.06,7.12)	6738 (6229,7109)	7.04 (6.99,7.11)	5.52 (5.46,5.6)	7464 (6695,8051)	0.06 (0.01,0.15)	3882 (3001,4388)	65765 (18961,387695)
65 year old Symptomatic Men	12.84 (12.41,13.15)	9.3 (8.73,9.69)	11019 (7803,15015)	13.12 (9.49,9.88)	9.69 (12.96,13.25)	12183 (10308,13944)	13.02 (12.68,13.24)	9.54 (9.1,9.84)	14294 (11350,17487)	0.26 (0.05,0.57)	2178 (-236,3650)	8367 (-389,67806)
65 year old Symptomatic Women	15.34 (14.9,15.69)	11.1 (10.54,11.55)	11674 (8430,15873)	15.64 (11.31,11.71)	11.51 (15.48,15.77)	12718 (10686,14506)	15.53 (15.19,15.78)	11.34 (10.91,11.68)	14974 (11781,17977)	0.26 (0.05,0.58)	2225 (-164,3712)	8491 (-638,60068)
70 year old Symptomatic Men	9.77 (9.5,9.96)	7.02 (6.68,7.27)	7676 (5472,10322)	9.94 (7.13,7.38)	7.26 (9.84,10.03)	9934 (8651,10981)	9.88 (9.66,10.02)	7.16 (6.88,7.36)	11536 (9585,13407)	0.17 (0.03,0.42)	2843 (732,3915)	16935 (1437,104691)
70 year old Symptomatic Women	11.8 (11.48,12)	8.46 (8.05,8.74)	8181 (5744,11346)	11.98 (8.58,8.85)	8.71 (11.87,12.07)	10365 (8846,11524)	11.91 (11.68,12.07)	8.6 (8.31,8.83)	12081 (9899,14077)	0.17 (0.03,0.42)	2870 (730,3953)	16836 (1595,139901)

75 year old Symptomatic Men	6.99 (6.82,7.12)	4.93 (4.71,5.1)	5485 (3936,7510)	7.1 (5.01,5.16)	5.08 (7.04,7.15)	8418 (7516,9092)	7.06 (6.93,7.15)	5.02 (4.86,5.14)	9641 (8145,10839)	0.11 (0.01,0.27)	3248 (1556,4179)	28483 (4512,212691)
75 year old Symptomatic Women	8.53 (8.31,8.68)	6.01 (5.73,6.22)	5804 (4042,8089)	8.64 (6.09,6.25)	6.17 (8.57,8.69)	8714 (7716,9433)	8.59 (8.44,8.69)	6.09 (5.92,6.24)	10016 (8392,11470)	0.12 (0.01,0.29)	3281 (1552,4208)	28452 (2057,189410)
80 year old Symptomatic Men	4.7 (4.6,4.77)	3.24 (3.12,3.33)	3348 (2410,4687)	4.75 (3.27,3.36)	3.31 (4.71,4.78)	7007 (6358,7465)	4.73 (4.65,4.78)	3.28 (3.18,3.35)	7887 (6830,8787)	0.06 (0,0.15)	3799 (2658,4417)	66299 (13751,496086)
80 year old Symptomatic Women	5.76 (5.66,5.84)	3.98 (3.85,4.08)	3527 (2512,4897)	5.81 (4.01,4.1)	4.06 (5.78,5.85)	7193 (6510,7633)	5.79 (5.71,5.84)	4.01 (3.91,4.09)	8124 (7089,9080)	0.06 (0,0.16)	3828 (2642,4427)	68305 (-346446,545863)

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]LYs, *QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using* ***DISCOUNTED*** *QALYs and lifetime costs*

Appendix Table 5.10: Deterministic sensitivity analyses (CEA and CAS costs from HRG reference costs) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Index cost of CEA: 4403; Index cost of CAS: 6595 (base case: CEA:4538 ; CAS:4752)	65 year old Asymptomatic Men	12.26 (11.82,12.61)	9290 (6760,12052)	12.7 (15.07,15.32)	10627 (9403,11595)	12.53 (12.23,12.81)	14301 (12314,16190)	0.26 (0.09,0.5)	2321 (534,3505)	9016 (1224,36806)
	65 year old Asymptomatic Women	14.15 (13.69,14.5)	9556 (7022,12790)	14.55 (17.37,17.61)	10895 (9539,11973)	14.39 (14.08,14.66)	14632 (12585,16629)	0.23 (0.08,0.47)	2423 (563,3459)	10506 (1366,43588)
	70 year old Asymptomatic Men	9.43 (9.13,9.65)	6539 (4776,8709)	9.7 (11.7,11.86)	8856 (7994,9565)	9.59 (9.38,9.78)	12110 (10700,13461)	0.18 (0.06,0.34)	2892 (1581,3710)	16442 (4560,58753)
	70 year old Asymptomatic Women	10.97 (10.68,11.2)	6766 (5088,8853)	11.22 (13.6,13.76)	9091 (8199,9805)	11.11 (10.9,11.29)	12396 (10970,13864)	0.16 (0.04,0.35)	2962 (1461,3804)	18633 (4120,88477)
	75 year old Asymptomatic Men	6.82 (6.61,6.99)	4700 (3491,6261)	7 (8.62,8.73)	7634 (7028,8201)	6.92 (6.79,7.05)	10579 (9578,11548)	0.13 (0.04,0.27)	3252 (2173,3910)	25848 (8002,98090)
	75 year old Asymptomatic Women	8 (7.79,8.16)	4839 (3666,6504)	8.17 (10.1,10.21)	7799 (7127,8299)	8.09 (7.95,8.22)	10779 (9715,11699)	0.11 (0.03,0.26)	3312 (2144,3974)	29220 (8169,125466)
	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2215,3927)	4.75 (6.01,6.07)	6508 (6126,6761)	4.7 (4.63,4.78)	9181 (8523,9709)	0.07 (0.02,0.16)	3709 (2906,4177)	54887 (17085,180566)
	80 year old Asymptomatic Women	5.49 (5.38,5.57)	3018 (2337,3991)	5.57 (7.05,7.12)	6613 (6213,6869)	5.52 (5.44,5.6)	9307 (8624,9853)	0.06 (0.01,0.15)	3757 (2969,4166)	63649 (18331,315834)
	65 year old Symptomatic Men	9.3 (8.7,9.69)	11019 (7858,15293)	9.69 (12.96,13.24)	12058 (10246,13640)	9.54 (9.1,9.86)	16136 (13196,19071)	0.26 (0.05,0.58)	2054 (-552,3549)	7887 (-1181,65715)
	65 year old Symptomatic Women	11.1 (10.52,11.54)	11674 (8173,15737)	11.51 (15.47,15.77)	12593 (10584,14194)	11.34 (10.86,11.68)	16817 (13781,19705)	0.26 (0.04,0.59)	2100 (-350,3531)	8015 (-904,67402)

	70 year old Symptomatic Men	7.02 (6.68,7.28)	7676 (5429,10534)	7.26 (9.85,10.03)	9809 (8539,10837)	7.16 (6.93,7.36)	13378 (11438,15151)	0.17 (0.02,0.39)	2718 (929,3794)	16191 (1861,132435)
	70 year old Symptomatic Women	8.46 (8.05,8.74)	8181 (5859,11508)	8.71 (11.88,12.07)	10240 (8909,11355)	8.6 (8.3,8.82)	13923 (11678,15961)	0.17 (0.02,0.41)	2745 (909,3839)	16103 (1154,120302)
	75 year old Symptomatic Men	4.93 (4.71,5.1)	5485 (3892,7534)	5.08 (7.04,7.16)	8294 (7328,8954)	5.02 (4.85,5.15)	11483 (9966,12774)	0.11 (0.02,0.28)	3123 (1377,3954)	27388 (4469,185535)
	75 year old Symptomatic Women	6.01 (5.74,6.2)	5804 (4082,8100)	6.17 (8.56,8.7)	8589 (7605,9313)	6.09 (5.91,6.24)	11859 (10160,13277)	0.12 (0.02,0.28)	3156 (1642,3967)	27369 (4973,185239)
	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2408,4861)	3.31 (4.71,4.78)	6882 (6317,7368)	3.28 (3.18,3.35)	9729 (8742,10619)	0.06 (0,0.15)	3674 (2627,4219)	64119 (10177,434206)
	80 year old Symptomatic Women	3.98 (3.85,4.08)	3527 (2450,4901)	4.06 (5.78,5.84)	7068 (6458,7451)	4.01 (3.92,4.09)	9966 (8968,10751)	0.06 (0,0.16)	3703 (2532,4245)	66077 (-189896,528106)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.11: Deterministic sensitivity analyses (increased in post-procedural stroke risks in asymptomatic patients by age and gender from ACAS, VA, ACST-) results: Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Increase in post-procedural stroke risks by age Symp: 1.38; Asymp: 1.72 (Base case: Symp: 1.38; Asymp: 1.38)	65 year old Asymptomatic Men	12.2 (11.62,12.51)	9775 (7496,13799)	12.65 (14.98,15.25)	11055 (9971,12541)	12.48 (12.06,12.72)	12829 (11051,15652)	0.27 (0.1,0.54)	2331 (258,3610)	8578 (512,32940)
	65 year old Asymptomatic Women	13.81 (13.47,14.39)	11903 (7822,14413)	14.35 (17.28,17.54)	12427 (10192,12936)	14.16 (13.93,14.57)	14466 (11227,16049)	0.31 (0.09,0.54)	1905 (275,3487)	6106 (387,33690)
	70 year old Asymptomatic Men	9.38 (9,9.58)	6913 (5445,9622)	9.67 (11.63,11.82)	9207 (8462,10269)	9.55 (9.28,9.73)	10546 (9244,12291)	0.19 (0.07,0.4)	2915 (1264,3790)	15501 (3436,53149)
	70 year old Asymptomatic Women	10.73 (10.53,11.1)	8488 (5575,9980)	11.09 (13.54,13.71)	10219 (8583,10493)	10.95 (10.81,11.26)	11758 (9430,12580)	0.22 (0.06,0.38)	2561 (1263,3812)	11490 (3239,68027)
	75 year old Asymptomatic Men	6.75 (6.46,6.9)	5220 (4038,7342)	6.96 (8.55,8.68)	8053 (7396,8865)	6.87 (6.68,7)	9087 (8089,10501)	0.15 (0.05,0.32)	3188 (1810,4027)	21478 (5842,72521)
	75 year old Asymptomatic Women	7.8 (7.64,8.08)	6374 (4188,7741)	8.06 (10.03,10.16)	8791 (7547,9039)	7.96 (7.84,8.17)	9971 (8261,10677)	0.18 (0.05,0.33)	2896 (1809,4007)	16357 (5588,84183)
	80 year old Asymptomatic Men	4.62 (4.46,4.71)	3279 (2572,4614)	4.73 (5.97,6.05)	6815 (6360,7341)	4.68 (4.56,4.75)	7557 (6895,8426)	0.08 (0.03,0.19)	3703 (2676,4243)	45289 (14191,143242)
	80 year old Asymptomatic Women	5.38 (5.28,5.54)	3987 (2672,4688)	5.51 (7.02,7.09)	7270 (6465,7430)	5.45 (5.41,5.57)	8104 (6993,8498)	0.1 (0.02,0.18)	3507 (2716,4306)	35318 (14504,205994)
	65 year old Symptomatic Men	9.3 (8.75,9.68)	11019 (8012,15058)	9.69 (12.97,13.25)	12183 (10343,13887)	9.54 (9.15,9.83)	14294 (11557,16910)	0.26 (0.06,0.56)	2178 (-195,3606)	8367 (-621,52509)
	65 year old Symptomatic Women	11.1 (10.55,11.53)	11674 (8326,15885)	11.51 (15.48,15.78)	12718 (10748,14321)	11.34 (10.93,11.68)	14974 (11985,17766)	0.26 (0.04,0.61)	2225 (-400,3727)	8491 (-1231,74459)

	70 year old Symptomatic Men	7.02 (6.66,7.28)	7676 (5603,10731)	7.26 (9.85,10.03)	9934 (8661,10962)	7.16 (6.9,7.36)	11536 (9441,13504)	0.17 (0.03,0.4)	2843 (937,3957)	16935 (1959,109275)
	70 year old Symptomatic Women	8.46 (8.05,8.73)	8181 (5904,11412)	8.71 (11.87,12.06)	10365 (8986,11520)	8.6 (8.31,8.81)	12081 (9964,14093)	0.17 (0.02,0.4)	2870 (866,3901)	16836 (1785,117853)
	75 year old Symptomatic Men	4.93 (4.7,5.11)	5485 (3843,7571)	5.08 (7.04,7.15)	8418 (7464,9120)	5.02 (4.83,5.15)	9641 (8136,11029)	0.11 (0.02,0.27)	3248 (1709,4109)	28483 (6082,162453)
	75 year old Symptomatic Women	6.01 (5.74,6.21)	5804 (4046,8085)	6.17 (8.57,8.69)	8714 (7681,9510)	6.09 (5.89,6.24)	10016 (8371,11416)	0.12 (0.01,0.27)	3281 (1767,4166)	28452 (4894,196346)
	80 year old Symptomatic Men	3.24 (3.11,3.34)	3348 (2332,4751)	3.31 (4.71,4.78)	7007 (6324,7484)	3.28 (3.2,3.35)	7887 (6924,8693)	0.06 (0,0.15)	3799 (2640,4449)	66299 (10351,547177)
	80 year old Symptomatic Women	3.98 (3.85,4.08)	3527 (2492,5049)	4.06 (5.78,5.84)	7193 (6502,7661)	4.01 (3.92,4.09)	8124 (7077,8966)	0.06 (0,0.15)	3828 (2658,4417)	68305 (-194273,499970)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.12: Deterministic sensitivity analyses (changes in relative post-procedural stroke risks of CAS vs CEA) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
CAS vs CEA post procedural major and minor stroke risks OR: 1.19 (base case: major strokes:1.23 ; minor stroke:1.54)	65 year old Asymptomatic Men	12.26 (11.84,12.6)	9290 (6922,12413)	12.7 (15.07,15.32)	10752 (9500,11804)	12.56 (12.26,12.82)	12268 (10435,14328)	0.26 (0.09,0.49)	2446 (629,3673)	9502 (1349,41554)
	65 year old Asymptomatic Women	14.15 (13.7,14.49)	9556 (7060,12704)	14.55 (17.37,17.6)	11020 (9673,12114)	14.41 (14.11,14.68)	12595 (10452,14545)	0.23 (0.07,0.47)	2548 (685,3660)	11047 (1482,44978)
	70 year old Asymptomatic Men	9.43 (9.11,9.67)	6539 (4769,8790)	9.7 (11.7,11.86)	8981 (8112,9760)	9.61 (9.41,9.79)	10136 (8747,11520)	0.18 (0.06,0.36)	3017 (1567,3942)	17152 (4592,62989)
	70 year old Asymptomatic Women	10.97 (10.68,11.2)	6766 (5071,8952)	11.22 (13.6,13.76)	9216 (8261,10008)	11.13 (10.91,11.31)	10419 (8929,11873)	0.16 (0.04,0.33)	3087 (1645,3980)	19419 (5144,95971)
	75 year old Asymptomatic Men	6.82 (6.62,6.97)	4700 (3514,6247)	7 (8.62,8.73)	7759 (7088,8284)	6.93 (6.8,7.05)	8642 (7629,9546)	0.13 (0.04,0.27)	3377 (2233,4136)	26840 (8146,100732)
	75 year old Asymptomatic Women	8 (7.79,8.17)	4839 (3561,6454)	8.17 (10.09,10.2)	7924 (7215,8419)	8.1 (7.97,8.23)	8841 (7741,9760)	0.11 (0.03,0.26)	3437 (2243,4147)	30321 (9296,121306)
	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2206,3964)	4.75 (6.01,6.07)	6633 (6120,7003)	4.71 (4.64,4.79)	7281 (6588,7845)	0.07 (0.01,0.15)	3833 (2989,4374)	56735 (20620,274833)
	80 year old Asymptomatic Women	5.49 (5.37,5.58)	3018 (2243,3949)	5.57 (7.05,7.12)	6738 (6220,7116)	5.53 (5.46,5.6)	7407 (6712,8067)	0.06 (0.01,0.15)	3882 (3028,4417)	65765 (16768,307565)
	65 year old Symptomatic Men	9.3 (8.76,9.69)	11019 (7948,15194)	9.69 (12.97,13.25)	12183 (10333,13813)	9.55 (9.17,9.86)	14102 (11394,16970)	0.26 (0.05,0.57)	2178 (-216,3635)	8367 (-541,66568)
	65 year old Symptomatic Women	11.1 (10.53,11.52)	11674 (8386,16232)	11.51 (15.49,15.77)	12718 (10726,14482)	11.36 (10.93,11.69)	14771 (11855,17364)	0.26 (0.03,0.57)	2225 (-308,3732)	8491 (-775,85524)

	70 year old Symptomatic Men	7.02 (6.64,7.28)	7676 (5527,10575)	7.26 (9.85,10.02)	9934 (8623,10931)	7.17 (6.92,7.38)	11402 (9347,13167)	0.17 (0.03,0.39)	2843 (887,3991)	16935 (1808,116333)
	70 year old Symptomatic Women	8.46 (8.08,8.74)	8181 (5786,11441)	8.71 (11.87,12.07)	10365 (9010,11492)	8.61 (8.35,8.83)	11939 (9799,13758)	0.17 (0.02,0.41)	2870 (854,4005)	16836 (1410,138497)
	75 year old Symptomatic Men	4.93 (4.69,5.09)	5485 (3991,7625)	5.08 (7.03,7.15)	8418 (7468,9174)	5.02 (4.86,5.15)	9545 (8088,10821)	0.11 (0.01,0.28)	3248 (1689,4110)	28483 (4591,178321)
	75 year old Symptomatic Women	6.01 (5.76,6.19)	5804 (4172,8245)	6.17 (8.57,8.69)	8714 (7604,9525)	6.1 (5.93,6.24)	9916 (8291,11385)	0.12 (0.02,0.28)	3281 (1709,4070)	28452 (4754,186889)
	80 year old Symptomatic Men	3.24 (3.11,3.33)	3348 (2447,4775)	3.31 (4.72,4.78)	7007 (6367,7528)	3.28 (3.19,3.35)	7829 (6844,8720)	0.06 (0,0.15)	3799 (2694,4390)	66299 (12067,425063)
	80 year old Symptomatic Women	3.98 (3.82,4.08)	3527 (2476,5105)	4.06 (5.78,5.85)	7193 (6518,7658)	4.02 (3.93,4.1)	8064 (7034,8891)	0.06 (0,0.16)	3828 (2718,4433)	68305 (-276814,431150)
CAS vs CEA post procedural major stroke risks OR: 1.05 and minor stroke risks OR: 2.58 as per results from ICSS (base case: majps strokes:1.23 ; minor stroke:1.54)	**65 year old Asymptomatic Men**	12.26 (11.84,12.63)	9290 (6744,12102)	12.7 (15.08,15.32)	10752 (9431,11784)	12.36 (12.05,12.67)	14732 (11960,17584)	0.26 (0.09,0.51)	2446 (741,3580)	9502 (1593,36217)
	65 year old Asymptomatic Women	14.15 (13.7,14.5)	9556 (6915,12694)	14.55 (17.37,17.6)	11020 (9743,12099)	14.23 (13.9,14.53)	15154 (12280,18425)	0.23 (0.07,0.47)	2548 (742,3721)	11047 (1548,48211)
	70 year old Asymptomatic Men	9.43 (9.14,9.67)	6539 (4872,8724)	9.7 (11.7,11.87)	8981 (8040,9749)	9.47 (9.24,9.68)	11820 (9929,14055)	0.18 (0.06,0.36)	3017 (1580,3916)	17152 (4620,66547)
	70 year old Asymptomatic Women	10.97 (10.67,11.21)	6766 (4972,8915)	11.22 (13.6,13.76)	9216 (8255,9979)	11 (10.78,11.19)	12171 (10138,14275)	0.16 (0.04,0.33)	3087 (1660,3982)	19419 (5413,90602)
	75 year old Asymptomatic Men	6.82 (6.6,6.97)	4700 (3544,6278)	7 (8.61,8.72)	7759 (7081,8317)	6.83 (6.68,6.99)	9821 (8373,11417)	0.13 (0.04,0.27)	3377 (2184,4102)	26840 (8196,107917)
	75 year old Asymptomatic Women	8 (7.81,8.17)	4839 (3563,6388)	8.17 (10.09,10.2)	7924 (7256,8450)	8.01 (7.86,8.15)	10057 (8511,11598)	0.11 (0.02,0.25)	3437 (2301,4186)	30321 (9315,161562)

	80 year old Asymptomatic Men	4.66 (4.55,4.75)	2948 (2213,3870)	4.75 (6.01,6.07)	6633 (6130,7022)	4.65 (4.57,4.74)	7987 (7041,8858)	0.07 (0.02,0.15)	3833 (3061,4380)	56735 (20486,217449)
	80 year old Asymptomatic Women	5.49 (5.37,5.58)	3018 (2258,3969)	5.57 (7.06,7.12)	6738 (6234,7113)	5.48 (5.39,5.56)	8124 (7215,9021)	0.06 (0.01,0.15)	3882 (2997,4355)	65765 (19888,312128)
	65 year old Symptomatic Men	9.3 (8.76,9.69)	11019 (7850,15033)	9.69 (12.97,13.25)	12183 (10390,13818)	9.55 (9.12,9.83)	15685 (12450,19097)	0.26 (0.04,0.59)	2178 (-426,3671)	8367 (-985,68979)
	65 year old Symptomatic Women	11.1 (10.46,11.53)	11674 (8497,15935)	11.51 (15.49,15.79)	12718 (10860,14221)	11.36 (10.97,11.66)	16479 (13005,19617)	0.26 (0.04,0.58)	2225 (-250,3725)	8491 (-833,53191)
	70 year old Symptomatic Men	7.02 (6.67,7.28)	7676 (5441,10552)	7.26 (9.85,10.02)	9934 (8689,10953)	7.17 (6.95,7.34)	12458 (10243,14435)	0.17 (0.03,0.4)	2843 (770,3968)	16935 (1503,99585)
	70 year old Symptomatic Women	8.46 (8.07,8.75)	8181 (5838,11361)	8.71 (11.88,12.07)	10365 (8908,11420)	8.61 (8.38,8.81)	13085 (10577,15313)	0.17 (0.02,0.39)	2870 (934,3985)	16836 (2269,109613)
	75 year old Symptomatic Men	4.93 (4.71,5.1)	5485 (3810,7577)	5.08 (7.04,7.15)	8418 (7453,9178)	5.02 (4.87,5.14)	10264 (8554,11888)	0.11 (0.02,0.26)	3248 (1758,4118)	28483 (5655,162782)
	75 year old Symptomatic Women	6.01 (5.74,6.19)	5804 (4140,8341)	6.17 (8.57,8.7)	8714 (7700,9540)	6.1 (5.93,6.23)	10690 (8913,12432)	0.12 (0.01,0.29)	3281 (1515,4206)	28452 (3145,185453)
	80 year old Symptomatic Men	3.24 (3.11,3.33)	3348 (2393,4760)	3.31 (4.72,4.78)	7007 (6327,7527)	3.28 (3.2,3.34)	8237 (7166,9193)	0.06 (0,0.16)	3799 (2655,4420)	66299 (-236228,378797)
	80 year old Symptomatic Women	3.98 (3.84,4.08)	3527 (2496,5038)	4.06 (5.78,5.84)	7193 (6527,7717)	4.01 (3.93,4.09)	8499 (7220,9446)	0.06 (0,0.16)	3828 (2689,4446)	68305 (-384116,818078)
CAS vs CEA post procedural minor stroke risks	**65 year old Asymptomatic Men**	12.26 (11.79,12.61)	9290 (6904,12352)	12.7 (15.07,15.32)	10752 (9467,11799)	12.58 (12.26,12.86)	11925 (9930,13748)	0.26 (0.09,0.51)	2446 (557,3625)	9502 (1248,38376)
	65 year old Asymptomatic Women	14.15 (13.68,14.48)	9556 (7151,12681)	14.55 (17.36,17.6)	11020 (9771,12208)	14.44 (14.11,14.7)	12242 (10301,14065)	0.23 (0.06,0.48)	2548 (685,3696)	11047 (1371,53613)

OR: 1 (base case: 1.54)	**70 year old Asymptomatic Men**	9.43 (9.12,9.64)	6539 (4847,8936)	9.7 (11.7,11.86)	8981 (8040,9707)	9.62 (9.44,9.81)	9905 (8528,11148)	0.18 (0.06,0.36)	3017 (1638,3920)	17152 (4747,67076)
	70 year old Asymptomatic Women	10.97 (10.66,11.18)	6766 (5051,8974)	11.22 (13.6,13.75)	9216 (8258,9897)	11.14 (10.95,11.32)	10180 (8846,11497)	0.16 (0.04,0.34)	3087 (1660,4033)	19419 (5113,90758)
	75 year old Asymptomatic Men	6.82 (6.63,6.98)	4700 (3524,6253)	7 (8.61,8.73)	7759 (7078,8227)	6.94 (6.81,7.07)	8483 (7428,9294)	0.13 (0.03,0.26)	3377 (2295,4176)	26840 (9295,123518)
	75 year old Asymptomatic Women	8 (7.8,8.15)	4839 (3649,6459)	8.17 (10.09,10.2)	7924 (7172,8507)	8.11 (7.97,8.24)	8678 (7601,9570)	0.11 (0.03,0.25)	3437 (2233,4152)	30321 (9069,135351)
	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2200,3934)	4.75 (6,6.07)	6633 (6095,7031)	4.72 (4.65,4.79)	7187 (6486,7738)	0.07 (0.02,0.15)	3833 (3017,4379)	56735 (20433,241497)
	80 year old Asymptomatic Women	5.49 (5.37,5.58)	3018 (2274,3994)	5.57 (7.06,7.12)	6738 (6214,7143)	5.54 (5.47,5.61)	7312 (6631,7902)	0.06 (0.01,0.15)	3882 (3063,4414)	65765 (20747,371846)
	65 year old Symptomatic Men	9.3 (8.77,9.68)	11019 (7787,14972)	9.69 (12.97,13.24)	12183 (10422,13757)	9.55 (9.15,9.84)	13908 (11181,16464)	0.26 (0.05,0.58)	2178 (-418,3666)	8367 (-995,60801)
	65 year old Symptomatic Women	11.1 (10.47,11.51)	11674 (8297,16345)	11.51 (15.46,15.77)	12718 (10778,14435)	11.36 (10.91,11.69)	14562 (11670,17395)	0.26 (0.05,0.62)	2225 (-385,3644)	8491 (-1035,60688)
	70 year old Symptomatic Men	7.02 (6.66,7.29)	7676 (5434,10605)	7.26 (9.85,10.03)	9934 (8660,11040)	7.17 (6.91,7.37)	11276 (9354,13059)	0.17 (0.02,0.41)	2843 (877,4034)	16935 (609,108393)
	70 year old Symptomatic Women	8.46 (8.06,8.74)	8181 (5684,11343)	8.71 (11.86,12.06)	10365 (8938,11487)	8.61 (8.34,8.82)	11802 (9634,13528)	0.17 (0.02,0.43)	2870 (791,3974)	16836 (1027,116583)
	75 year old Symptomatic Men	4.93 (4.69,5.1)	5485 (3851,7627)	5.08 (7.03,7.15)	8418 (7447,9228)	5.02 (4.83,5.15)	9461 (7976,10856)	0.11 (0.02,0.27)	3248 (1765,4082)	28483 (6400,184311)
	75 year old Symptomatic Women	6.01 (5.76,6.21)	5804 (4102,8030)	6.17 (8.57,8.7)	8714 (7703,9552)	6.1 (5.92,6.25)	9825 (8260,11229)	0.12 (0.01,0.28)	3281 (1726,4209)	28452 (5616,234050)

	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2348,4674)	3.31 (4.72,4.78)	7007 (6335,7461)	3.28 (3.2,3.35)	7783 (6794,8563)	0.06 (0,0.15)	3799 (2700,4437)	66299 (10400,621831)
	80 year old Symptomatic Women	3.98 (3.85,4.08)	3527 (2557,4898)	4.06 (5.78,5.84)	7193 (6515,7695)	4.02 (3.92,4.1)	8014 (6943,8858)	0.06 (-0.01,0.15)	3828 (2736,4463)	68305 (-259793,572417)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.13: Deterministic sensitivity analyses (changes in relative procedural stroke risks by age) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Increase in post-procedural stroke risks by age Symp: 1.38; Asymp: 1.72 (Base case: Symp: 1.38; Asymp: 1.38)	65 year old Asymptomatic Men	12.26 (11.81,12.6)	9290 (6871,12476)	12.7 (15.08,15.32)	10752 (9501,11886)	12.57 (12.24,12.83)	12167 (10329,14282)	0.26 (0.09,0.51)	2446 (618,3628)	9502 (1343,41143)
	65 year old Asymptomatic Women	14.15 (13.69,14.49)	9556 (7015,13079)	14.55 (17.37,17.6)	11020 (9615,12191)	14.43 (14.09,14.69)	12447 (10497,14835)	0.23 (0.08,0.45)	2548 (804,3644)	11047 (1675,44786)
	70 year old Asymptomatic Men	9.43 (9.13,9.66)	6539 (4839,8779)	9.7 (11.7,11.86)	8981 (8026,9730)	9.55 (9.34,9.74)	10448 (8998,11887)	0.18 (0.06,0.36)	3017 (1610,3854)	17152 (4616,59822)
	70 year old Asymptomatic Women	10.97 (10.68,11.2)	6766 (5108,8992)	11.22 (13.6,13.76)	9216 (8291,9987)	11.07 (10.87,11.28)	10761 (9210,12030)	0.16 (0.05,0.34)	3087 (1606,3891)	19419 (4995,73338)
	75 year old Asymptomatic Men	6.82 (6.65,6.98)	4700 (3421,6191)	7 (8.61,8.73)	7759 (7080,8335)	6.89 (6.77,7.03)	8886 (7783,9853)	0.13 (0.04,0.26)	3377 (2243,4177)	26840 (8871,101677)
	75 year old Asymptomatic Women	8 (7.78,8.16)	4839 (3602,6452)	8.17 (10.1,10.21)	7924 (7208,8447)	8.06 (7.93,8.2)	9107 (7919,9977)	0.11 (0.03,0.24)	3437 (2262,4154)	30321 (9560,134314)
	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2203,3935)	4.75 (6.01,6.07)	6633 (6143,6991)	4.68 (4.61,4.76)	7463 (6745,8115)	0.07 (0.02,0.15)	3833 (3054,4360)	56735 (20413,259431)
	80 year old Asymptomatic Women	5.49 (5.38,5.58)	3018 (2245,4002)	5.57 (7.05,7.12)	6738 (6170,7133)	5.5 (5.41,5.58)	7603 (6849,8259)	0.06 (0.01,0.14)	3882 (3083,4375)	65765 (21990,410346)
	65 year old Symptomatic Men	9.3 (8.76,9.68)	11019 (7834,14913)	9.69 (12.97,13.26)	12183 (10337,13699)	9.57 (9.17,9.86)	13797 (11300,16890)	0.26 (0.05,0.59)	2178 (-359,3634)	8367 (-792,61188)
	65 year old Symptomatic Women	11.1 (10.46,11.54)	11674 (8296,16448)	11.51 (15.48,15.78)	12718 (10654,14470)	11.38 (10.98,11.7)	14390 (11553,17419)	0.26 (0.05,0.59)	2225 (-327,3665)	8491 (-623,59887)

	70 year old Symptomatic Men	7.02 (6.66,7.26)	7676 (5588,10660)	7.26 (9.85,10.02)	9934 (8654,10946)	7.12 (6.87,7.32)	11846 (9735,13622)	0.17 (0.02,0.39)	2843 (927,4075)	16935 (2012,140995)
	70 year old Symptomatic Women	8.46 (8.09,8.75)	8181 (5865,11198)	8.71 (11.88,12.07)	10365 (8947,11501)	8.55 (8.28,8.76)	12437 (10223,14429)	0.17 (0.02,0.44)	2870 (781,4041)	16836 (1044,111294)
	75 year old Symptomatic Men	4.93 (4.71,5.09)	5485 (3873,7493)	5.08 (7.04,7.15)	8418 (7487,9115)	4.99 (4.82,5.12)	9900 (8276,11151)	0.11 (0.01,0.27)	3248 (1763,4194)	28483 (5131,206594)
	75 year old Symptomatic Women	6.01 (5.74,6.2)	5804 (4065,7950)	6.17 (8.56,8.69)	8714 (7682,9516)	6.06 (5.86,6.2)	10310 (8700,11721)	0.12 (0,0.27)	3281 (1684,4265)	28452 (2034,196444)
	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2398,4631)	3.31 (4.72,4.78)	7007 (6365,7489)	3.26 (3.17,3.33)	8105 (7110,8850)	0.06 (0,0.15)	3799 (2756,4369)	66299 (15412,450922)
	80 year old Symptomatic Women	3.98 (3.85,4.08)	3527 (2513,4902)	4.06 (5.78,5.85)	7193 (6469,7658)	3.99 (3.9,4.07)	8367 (7192,9168)	0.06 (0,0.15)	3828 (2738,4435)	68305 (-315978,578696)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.14: Deterministic sensitivity analyses (changes in procedural stroke/death risks of CEA) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Procedural stroke/death of CEA: Asymp:3%; Symp:6% (base case: Asymp: 1.50%; Symp: 2.68%)	65 year old Asymptomatic Men	12.26 (11.82,12.6)	9290 (6842,12506)	12.63 (15.04,15.27)	11169 (9772,12109)	12.42 (12.15,12.74)	13172 (10902,15033)	0.21 (0.05,0.48)	2798 (925,3908)	13445 (2282,69178)
	65 year old Asymptomatic Women	14.15 (13.68,14.48)	9556 (7160,12971)	14.48 (17.31,17.56)	11506 (10008,12553)	14.28 (13.99,14.59)	13628 (11128,15480)	0.18 (0.03,0.43)	2945 (821,3992)	16493 (1488,89445)
	70 year old Asymptomatic Men	9.43 (9.12,9.67)	6539 (4856,8645)	9.65 (11.66,11.83)	9327 (8248,9990)	9.5 (9.31,9.73)	10859 (9138,11962)	0.13 (0.01,0.32)	3323 (1880,4158)	24778 (5337,170815)
	70 year old Asymptomatic Women	10.97 (10.64,11.19)	6766 (5056,9048)	11.16 (13.56,13.72)	9617 (8455,10231)	11.02 (10.85,11.23)	11245 (9425,12229)	0.11 (0,0.3)	3431 (1840,4333)	30057 (-125670,212757)
	75 year old Asymptomatic Men	6.82 (6.61,6.98)	4700 (3415,6253)	6.96 (8.58,8.7)	8036 (7213,8497)	6.85 (6.73,7.01)	9209 (7881,10032)	0.09 (0.01,0.24)	3632 (2382,4279)	39385 (8703,260983)
	75 year old Asymptomatic Women	8 (7.77,8.16)	4839 (3574,6476)	8.12 (10.06,10.17)	8244 (7422,8702)	8.02 (7.88,8.18)	9485 (8150,10300)	0.08 (-0.01,0.23)	3725 (2426,4358)	48482 (-139205,303508)
	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2207,3945)	4.72 (5.98,6.05)	6855 (6287,7163)	4.65 (4.59,4.75)	7715 (6851,8221)	0.04 (-0.01,0.14)	4045 (3121,4505)	96726 (-477504,783637)
	80 year old Asymptomatic Women	5.49 (5.38,5.58)	3018 (2296,4024)	5.54 (7.03,7.1)	6989 (6345,7331)	5.47 (5.4,5.57)	7894 (6970,8390)	0.03 (-0.02,0.12)	4117 (3254,4574)	134028 (-614104,795679)
	65 year old Symptomatic Men	9.3 (8.77,9.69)	11019 (7920,14821)	9.6 (12.92,13.21)	13070 (10845,14365)	9.41 (9.04,9.75)	15801 (12204,17880)	0.19 (-0.02,0.52)	2930 (238,4229)	15419 (-103382,186654)
	65 year old Symptomatic Women	11.1 (10.47,11.54)	11674 (8215,15794)	11.41 (15.39,15.72)	13750 (11303,15168)	11.18 (10.73,11.56)	16741 (12826,19515)	0.18 (-0.02,0.55)	3070 (235,4133)	17040 (-106973,158215)

	70 year old Symptomatic Men	7.02 (6.7,7.27)	7676 (5620,10462)	7.19 (9.8,9.99)	10676 (9081,11597)	7.06 (6.81,7.28)	12798 (10140,14217)	0.11 (-0.03,0.35)	3498 (1323,4418)	31479 (-262699,311499)
	70 year old Symptomatic Women	8.46 (8.07,8.75)	8181 (5766,11157)	8.63 (11.82,12.01)	11225 (9445,12076)	8.48 (8.24,8.73)	13554 (10665,14832)	0.1 (-0.05,0.34)	3608 (1415,4560)	34831 (-288276,392533)
	75 year old Symptomatic Men	4.93 (4.68,5.1)	5485 (3928,7746)	5.03 (7,7.12)	9017 (7832,9686)	4.94 (4.78,5.09)	10654 (8666,11841)	0.07 (-0.03,0.25)	3798 (1999,4565)	52832 (-406671,460003)
	75 year old Symptomatic Women	6.01 (5.73,6.18)	5804 (4217,8336)	6.11 (8.53,8.66)	9403 (8064,10010)	6 (5.83,6.17)	11192 (9002,12340)	0.06 (-0.05,0.25)	3900 (1997,4686)	60195 (-500735,483445)
	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2448,4700)	3.28 (4.7,4.76)	7490 (6637,7832)	3.23 (3.15,3.31)	8703 (7309,9304)	0.03 (-0.02,0.13)	4258 (2918,4717)	153615 (-1217929,1863443)
	80 year old Symptomatic Women	3.98 (3.86,4.08)	3527 (2461,4909)	4.01 (5.75,5.82)	7740 (6781,8098)	3.95 (3.85,4.05)	9053 (7552,9639)	0.02 (-0.04,0.13)	4340 (2874,4880)	214870 (-1559830,1829274)
Procedural stroke/death of CEA: Asymp:2.7%; Symp:5.4% (base case: Asymp: 1.50%; Symp: 2.68%)	**65 year old Asymptomatic Men**	12.26 (11.79,12.61)	9290 (6888,12087)	12.76 (15.12,15.37)	10335 (9275,11477)	12.64 (12.31,12.88)	11744 (10155,14016)	0.22 (0.06,0.47)	2728 (727,3836)	12514 (1445,55777)
	65 year old Asymptomatic Women	14.15 (13.68,14.48)	9556 (7064,12668)	14.62 (17.43,17.65)	10534 (9416,11699)	14.51 (14.16,14.75)	11952 (10229,14417)	0.19 (0.02,0.42)	2865 (943,3964)	15163 (1903,86847)
	70 year old Asymptomatic Men	9.43 (9.13,9.66)	6539 (4841,8681)	9.76 (11.74,11.89)	8636 (7876,9411)	9.67 (9.45,9.83)	9676 (8518,11160)	0.14 (0.02,0.34)	3262 (1786,4147)	22895 (5408,115174)
	70 year old Asymptomatic Women	10.97 (10.67,11.2)	6766 (4964,8924)	11.28 (13.64,13.8)	8815 (8000,9575)	11.2 (11,11.37)	9862 (8676,11371)	0.12 (0.01,0.32)	3362 (1790,4165)	27310 (4666,213950)
	75 year old Asymptomatic Men	6.82 (6.61,6.98)	4700 (3477,6270)	7.04 (8.65,8.76)	7481 (6905,8092)	6.99 (6.83,7.09)	8264 (7446,9391)	0.1 (0.02,0.25)	3581 (2294,4285)	36194 (8313,176910)
	75 year old Asymptomatic Women	8 (7.8,8.14)	4839 (3661,6311)	8.21 (10.12,10.23)	7605 (6976,8268)	8.16 (8.01,8.27)	8388 (7518,9522)	0.08 (0.01,0.23)	3667 (2398,4276)	43588 (9536,298525)

	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2211,3927)	4.78 (6.03,6.09)	6411 (5993,6827)	4.75 (4.67,4.81)	6963 (6399,7660)	0.05 (-0.01,0.14)	4002 (3114,4462)	85219 (-288581,686986)
	80 year old Asymptomatic Women	5.49 (5.37,5.57)	3018 (2287,4100)	5.6 (7.08,7.14)	6486 (6054,6913)	5.58 (5.49,5.63)	7035 (6472,7791)	0.04 (-0.02,0.13)	4070 (3200,4560)	111877 (-479604,806359)
	65 year old Symptomatic Men	9.3 (8.78,9.71)	11019 (7884,14782)	9.76 (13,13.29)	11467 (9867,13293)	9.64 (9.2,9.94)	13078 (10664,16310)	0.2 (0,0.5)	2794 (329,4083)	13782 (-1131,107522)
	65 year old Symptomatic Women	11.1 (10.48,11.54)	11674 (8106,16291)	11.6 (15.52,15.83)	11884 (10210,13977)	11.47 (10.97,11.78)	13548 (11142,17123)	0.19 (-0.03,0.57)	2917 (148,4200)	14964 (-89081,163367)
	70 year old Symptomatic Men	7.02 (6.68,7.27)	7676 (5492,10513)	7.32 (9.88,10.06)	9334 (8268,10555)	7.24 (6.98,7.42)	10517 (8942,12748)	0.12 (-0.01,0.36)	3380 (1169,4380)	27845 (-159294,326157)
	70 year old Symptomatic Women	8.46 (8.05,8.75)	8181 (5888,11389)	8.78 (11.92,12.1)	9671 (8584,10867)	8.7 (8.39,8.91)	10892 (9142,13430)	0.12 (-0.03,0.34)	3475 (1383,4437)	30039 (-264334,290111)
	75 year old Symptomatic Men	4.93 (4.69,5.1)	5485 (3923,7697)	5.12 (7.06,7.18)	7935 (7166,8793)	5.07 (4.89,5.19)	8823 (7675,10426)	0.08 (-0.02,0.25)	3699 (1966,4449)	46520 (-230851,420615)
	75 year old Symptomatic Women	6.01 (5.75,6.19)	5804 (4152,8404)	6.22 (8.6,8.72)	8158 (7344,9086)	6.16 (5.97,6.29)	9067 (7929,10893)	0.07 (-0.04,0.26)	3788 (1913,4643)	51247 (-405624,627889)
	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2399,4703)	3.34 (4.73,4.79)	6617 (6100,7210)	3.32 (3.23,3.37)	7228 (6509,8258)	0.03 (-0.02,0.13)	4175 (2945,4733)	126268 (-1037543,962898)
	80 year old Symptomatic Women	3.98 (3.85,4.07)	3527 (2481,4837)	4.09 (5.8,5.86)	6751 (6214,7339)	4.06 (3.96,4.13)	7373 (6635,8349)	0.03 (-0.03,0.14)	4247 (2925,4811)	159220 (-1260638,1485531)
Procedural stroke/death of CEA: Asymp:2.4%; Symp:4.8% (base case:	**65 year old Asymptomatic Men**	12.26 (11.82,12.61)	9290 (6859,12674)	12.76 (15.11,15.36)	10335 (9224,11615)	12.64 (12.3,12.88)	11744 (10093,14049)	0.23 (0.07,0.48)	2657 (898,3758)	11663 (1993,52055)
	65 year old Asymptomatic Women	14.15 (13.67,14.49)	9556 (7057,12689)	14.62 (17.42,17.65)	10534 (9420,11742)	14.51 (14.17,14.76)	11952 (10199,14265)	0.2 (0.05,0.47)	2786 (673,3856)	13973 (979,60296)

Asymp: 1.50%; Symp: 2.68%)	**70 year old Asymptomatic Men**	9.43 (9.16,9.68)	6539 (4800,8664)	9.76 (11.73,11.89)	8636 (7849,9494)	9.67 (9.43,9.84)	9676 (8471,11307)	0.15 (0.04,0.34)	3201 (1764,3991)	21220 (5515,93721)
	70 year old Asymptomatic Women	10.97 (10.66,11.19)	6766 (5054,9127)	11.28 (13.63,13.79)	8815 (8084,9658)	11.2 (10.96,11.35)	9862 (8724,11480)	0.13 (0.02,0.3)	3294 (1849,4169)	24936 (6016,138200)
	75 year old Asymptomatic Men	6.82 (6.62,6.98)	4700 (3500,6237)	7.04 (8.64,8.75)	7481 (6883,8067)	6.99 (6.84,7.09)	8264 (7470,9502)	0.11 (0.02,0.26)	3530 (2321,4204)	33410 (8850,231697)
	75 year old Asymptomatic Women	8 (7.81,8.16)	4839 (3622,6493)	8.21 (10.13,10.23)	7605 (6996,8177)	8.16 (8.02,8.27)	8388 (7508,9528)	0.09 (0,0.23)	3610 (2395,4304)	39476 (5942,207886)
	80 year old Asymptomatic Men	4.66 (4.55,4.75)	2948 (2134,3855)	4.78 (6.03,6.09)	6411 (5975,6818)	4.75 (4.67,4.81)	6963 (6395,7697)	0.05 (0,0.14)	3960 (3088,4486)	75987 (-145128,490276)
	80 year old Asymptomatic Women	5.49 (5.38,5.58)	3018 (2268,4032)	5.6 (7.08,7.14)	6486 (6035,6944)	5.58 (5.5,5.64)	7035 (6467,7735)	0.04 (-0.01,0.13)	4023 (3180,4547)	95692 (-396463,975798)
	65 year old Symptomatic Men	9.3 (8.78,9.68)	11019 (7873,15224)	9.76 (13.02,13.29)	11467 (9880,13234)	9.64 (9.22,9.91)	13078 (10801,16281)	0.22 (0,0.56)	2658 (16,4007)	12338 (-73860,92886)
	65 year old Symptomatic Women	11.1 (10.48,11.53)	11674 (8355,16304)	11.6 (15.53,15.83)	11884 (10320,13880)	11.47 (10.99,11.78)	13548 (11159,16963)	0.21 (-0.01,0.56)	2764 (-161,4094)	13180 (-93691,154914)
	70 year old Symptomatic Men	7.02 (6.69,7.29)	7676 (5528,10302)	7.32 (9.87,10.06)	9334 (8247,10523)	7.24 (6.97,7.44)	10517 (8871,12777)	0.13 (-0.01,0.35)	3261 (1365,4214)	24776 (-121537,192706)
	70 year old Symptomatic Women	8.46 (8.1,8.74)	8181 (5733,11074)	8.78 (11.92,12.1)	9671 (8573,10923)	8.7 (8.41,8.9)	10892 (9207,13327)	0.13 (-0.02,0.37)	3341 (1153,4247)	26154 (-204402,342937)
	75 year old Symptomatic Men	4.93 (4.69,5.1)	5485 (3857,7823)	5.12 (7.06,7.17)	7935 (7150,8783)	5.07 (4.9,5.19)	8823 (7623,10432)	0.09 (-0.01,0.24)	3599 (2008,4403)	41312 (-181446,390087)
	75 year old Symptomatic Women	6.01 (5.78,6.2)	5804 (4023,8003)	6.22 (8.6,8.72)	8158 (7351,9043)	6.16 (5.96,6.29)	9067 (7845,10701)	0.08 (-0.02,0.28)	3676 (1912,4509)	44265 (-352949,411751)

	80 year old Symptomatic Men	3.24 (3.1,3.33)	3348 (2409,4879)	3.34 (4.73,4.79)	6617 (6102,7222)	3.32 (3.22,3.37)	7228 (6468,8251)	0.04 (-0.02,0.14)	4092 (2880,4701)	106534 (-1090040,989631)
	80 year old Symptomatic Women	3.98 (3.84,4.08)	3527 (2501,5081)	4.09 (5.8,5.86)	6751 (6244,7336)	4.06 (3.95,4.13)	7373 (6634,8437)	0.03 (-0.02,0.14)	4155 (2852,4699)	125318 (-888410,1040088)
Procedural stroke/death of CEA: Asymp:2.1%; Symp:4.2% (base case: Asymp: 1.50%; Symp: 2.68%)	**65 year old Asymptomatic Men**	12.26 (11.83,12.6)	9290 (7008,12152)	12.76 (15.11,15.36)	10335 (9320,11550)	12.64 (12.28,12.89)	11744 (10056,14119)	0.24 (0.09,0.48)	2587 (654,3711)	10883 (1361,40721)
	65 year old Asymptomatic Women	14.15 (13.69,14.48)	9556 (7059,12715)	14.62 (17.42,17.65)	10534 (9461,11681)	14.51 (14.17,14.75)	11952 (10163,14450)	0.21 (0.06,0.47)	2707 (708,3811)	12901 (1473,61675)
	70 year old Asymptomatic Men	9.43 (9.12,9.66)	6539 (4899,8787)	9.76 (11.73,11.89)	8636 (7845,9489)	9.67 (9.44,9.84)	9676 (8492,11203)	0.16 (0.05,0.35)	3139 (1722,3988)	19722 (4748,78565)
	70 year old Asymptomatic Women	10.97 (10.65,11.19)	6766 (5112,9063)	11.28 (13.64,13.79)	8815 (8008,9619)	11.2 (10.99,11.37)	9862 (8545,11427)	0.14 (0.03,0.33)	3225 (1715,4071)	22863 (4200,96594)
	75 year old Asymptomatic Men	6.82 (6.6,6.98)	4700 (3540,6305)	7.04 (8.64,8.75)	7481 (6898,8076)	6.99 (6.83,7.1)	8264 (7404,9373)	0.11 (0.03,0.26)	3479 (2276,4171)	30958 (8858,129751)
	75 year old Asymptomatic Women	8 (7.81,8.16)	4839 (3552,6343)	8.21 (10.13,10.23)	7605 (6945,8120)	8.16 (8,8.27)	8388 (7505,9521)	0.1 (0.01,0.24)	3552 (2327,4294)	35973 (8963,268532)
	80 year old Asymptomatic Men	4.66 (4.53,4.75)	2948 (2164,3986)	4.78 (6.03,6.09)	6411 (6016,6853)	4.75 (4.66,4.81)	6963 (6407,7736)	0.06 (0,0.15)	3918 (3057,4427)	68415 (18271,427145)
	80 year old Asymptomatic Women	5.49 (5.38,5.58)	3018 (2272,3947)	5.6 (7.08,7.14)	6486 (6060,6956)	5.58 (5.49,5.64)	7035 (6421,7788)	0.05 (-0.01,0.13)	3976 (3196,4489)	83348 (-436962,581220)
	65 year old Symptomatic Men	9.3 (8.77,9.67)	11019 (7965,14877)	9.76 (13.02,13.3)	11467 (9902,13218)	9.64 (9.2,9.93)	13078 (10749,16558)	0.23 (0.03,0.54)	2522 (-74,3832)	11056 (-608,68917)
	65 year old Symptomatic Women	11.1 (10.49,11.52)	11674 (8291,15914)	11.6 (15.52,15.83)	11884 (10269,13749)	11.47 (10.95,11.8)	13548 (11125,17066)	0.22 (0,0.55)	2612 (79,3936)	11632 (-51009,91767)

	70 year old Symptomatic Men	7.02 (6.69,7.29)	7676 (5508,10402)	7.32 (9.88,10.06)	9334 (8254,10566)	7.24 (6.97,7.42)	10517 (8826,12601)	0.14 (0.01,0.36)	3143 (1120,4128)	22151 (1476,172451)
	70 year old Symptomatic Women	8.46 (8.12,8.76)	8181 (5830,11255)	8.78 (11.91,12.11)	9671 (8580,10978)	8.7 (8.4,8.9)	10892 (9227,13229)	0.14 (-0.02,0.38)	3208 (1074,4300)	22939 (-200614,201749)
	75 year old Symptomatic Men	4.93 (4.69,5.1)	5485 (3864,7618)	5.12 (7.06,7.17)	7935 (7162,8807)	5.07 (4.9,5.19)	8823 (7645,10474)	0.09 (0,0.27)	3500 (1797,4310)	36942 (-194888,302523)
	75 year old Symptomatic Women	6.01 (5.73,6.19)	5804 (4072,8239)	6.22 (8.6,8.72)	8158 (7341,9094)	6.16 (5.98,6.3)	9067 (7800,10698)	0.09 (-0.02,0.28)	3564 (1751,4392)	38667 (-427312,604006)
	80 year old Symptomatic Men	3.24 (3.12,3.32)	3348 (2398,4798)	3.34 (4.73,4.79)	6617 (6086,7214)	3.32 (3.2,3.38)	7228 (6528,8453)	0.04 (-0.01,0.14)	4009 (2844,4564)	91622 (-894405,787068)
	80 year old Symptomatic Women	3.98 (3.84,4.08)	3527 (2477,4999)	4.09 (5.8,5.86)	6751 (6193,7340)	4.06 (3.95,4.13)	7373 (6633,8452)	0.04 (-0.02,0.14)	4062 (2857,4581)	102500 (-837977,894129)
Procedural stroke/death of CEA: Asymp:1.8%; Symp:3.6% (base case: Asymp: 1.50%; Symp: 2.68%)	**65 year old Asymptomatic Men**	12.26 (11.82,12.59)	9290 (6941,12117)	12.76 (15.12,15.36)	10335 (9191,11363)	12.64 (12.29,12.88)	11744 (9998,13857)	0.25 (0.08,0.5)	2516 (739,3722)	10165 (1522,43611)
	65 year old Asymptomatic Women	14.15 (13.67,14.49)	9556 (7124,12907)	14.62 (17.42,17.65)	10534 (9326,11823)	14.51 (14.17,14.74)	11952 (10322,14314)	0.22 (0.06,0.46)	2628 (708,3797)	11930 (1329,54778)
	70 year old Asymptomatic Men	9.43 (9.12,9.65)	6539 (4870,8731)	9.76 (11.74,11.9)	8636 (7886,9414)	9.67 (9.45,9.84)	9676 (8510,11227)	0.17 (0.05,0.36)	3078 (1607,3971)	18373 (4297,74650)
	70 year old Asymptomatic Women	10.97 (10.64,11.2)	6766 (4978,9047)	11.28 (13.63,13.79)	8815 (8039,9694)	11.2 (10.97,11.37)	9862 (8688,11354)	0.15 (0.05,0.34)	3156 (1738,3978)	21038 (5458,80454)
	75 year old Asymptomatic Men	6.82 (6.6,6.97)	4700 (3551,6322)	7.04 (8.64,8.75)	7481 (6928,8159)	6.99 (6.84,7.09)	8264 (7367,9429)	0.12 (0.03,0.27)	3428 (2190,4160)	28783 (8174,129434)
	75 year old Asymptomatic Women	8 (7.79,8.16)	4839 (3576,6480)	8.21 (10.13,10.24)	7605 (6980,8168)	8.16 (8.01,8.28)	8388 (7508,9584)	0.11 (0.02,0.24)	3495 (2269,4231)	32952 (8332,161911)

	80 year old Asymptomatic Men	4.66 (4.54,4.75)	2948 (2203,4053)	4.78 (6.03,6.09)	6411 (5985,6869)	4.75 (4.67,4.81)	6963 (6378,7643)	0.06 (0.01,0.14)	3876 (3109,4418)	62093 (18373,253014)
	80 year old Asymptomatic Women	5.49 (5.38,5.58)	3018 (2273,3962)	5.6 (7.08,7.14)	6486 (6050,6930)	5.58 (5.5,5.63)	7035 (6522,7749)	0.05 (0,0.14)	3929 (3101,4414)	73624 (19650,389022)
	65 year old Symptomatic Men	9.3 (8.71,9.72)	11019 (7844,15299)	9.76 (13.01,13.3)	11467 (9990,13397)	9.64 (9.19,9.91)	13078 (10828,16442)	0.24 (0.03,0.53)	2387 (7,3841)	9908 (-513,83472)
	65 year old Symptomatic Women	11.1 (10.52,11.55)	11674 (8270,16014)	11.6 (15.52,15.84)	11884 (10306,13674)	11.47 (11.01,11.79)	13548 (11117,16805)	0.24 (0.02,0.58)	2459 (-240,3860)	10275 (-1204,100438)
	70 year old Symptomatic Men	7.02 (6.67,7.3)	7676 (5476,10376)	7.32 (9.88,10.06)	9334 (8261,10540)	7.24 (6.97,7.42)	10517 (8899,12767)	0.15 (0,0.36)	3024 (1106,4162)	19879 (1771,250586)
	70 year old Symptomatic Women	8.46 (8.09,8.74)	8181 (5848,11239)	8.78 (11.91,12.1)	9671 (8483,10982)	8.7 (8.39,8.9)	10892 (9205,13265)	0.15 (0.01,0.42)	3074 (896,4169)	20236 (432,148340)
	75 year old Symptomatic Men	4.93 (4.68,5.1)	5485 (3880,7723)	5.12 (7.06,7.17)	7935 (7164,8801)	5.07 (4.87,5.19)	8823 (7596,10584)	0.1 (0,0.26)	3401 (1751,4279)	33222 (-42,229199)
	75 year old Symptomatic Women	6.01 (5.77,6.19)	5804 (4135,8163)	6.22 (8.6,8.72)	8158 (7333,9031)	6.16 (5.96,6.29)	9067 (7902,10885)	0.1 (0,0.29)	3452 (1631,4266)	34078 (-118493,320192)
	80 year old Symptomatic Men	3.24 (3.12,3.33)	3348 (2381,4698)	3.34 (4.73,4.79)	6617 (6093,7169)	3.32 (3.22,3.38)	7228 (6505,8171)	0.05 (0,0.15)	3926 (2631,4498)	79957 (-614227,724954)
	80 year old Symptomatic Women	3.98 (3.83,4.07)	3527 (2550,5039)	4.09 (5.8,5.86)	6751 (6229,7324)	4.06 (3.96,4.13)	7373 (6639,8446)	0.05 (-0.01,0.14)	3970 (2754,4540)	86094 (-715685,787946)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.15: Deterministic sensitivity analyses (fatalities in major strokes) results:

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Fatalities in major strokes = 15% (base case: 32.35%)	65 year old Asymptomatic Men	12.4 (12.03,12.72)	10150 (7595,13448)	12.78 (15.26,15.43)	11273 (9951,12430)	12.63 (12.35,12.87)	13090 (10969,15388)	0.22 (0.08,0.43)	2218 (112,3523)	9964 (252,42408)
	65 year old Asymptomatic Women	14.29 (13.91,14.59)	10412 (7608,13845)	14.64 (17.56,17.72)	11544 (10057,12839)	14.5 (14.24,14.73)	13427 (11146,15759)	0.2 (0.07,0.42)	2336 (304,3649)	11818 (702,51308)
	70 year old Asymptomatic Men	9.51 (9.25,9.72)	7121 (5189,9571)	9.75 (11.82,11.93)	9339 (8302,10139)	9.65 (9.46,9.81)	10703 (9157,12402)	0.15 (0.05,0.32)	2856 (1229,3824)	18568 (3904,72603)
	70 year old Asymptomatic Women	11.05 (10.81,11.26)	7347 (5498,9603)	11.28 (13.72,13.83)	9579 (8585,10473)	11.18 (11.01,11.35)	10996 (9359,12422)	0.14 (0.04,0.3)	2936 (1280,3983)	21312 (4274,90662)
	75 year old Asymptomatic Men	6.87 (6.69,7.01)	5109 (3828,7071)	7.03 (8.69,8.77)	8013 (7257,8604)	6.96 (6.85,7.08)	9046 (7909,10174)	0.11 (0.04,0.22)	3255 (2088,4033)	29328 (9382,94457)
	75 year old Asymptomatic Women	8.06 (7.89,8.21)	5245 (3847,6893)	8.2 (10.18,10.25)	8181 (7420,8835)	8.13 (8.01,8.25)	9250 (8029,10402)	0.1 (0.03,0.21)	3324 (2107,4169)	33545 (9706,141045)
	80 year old Asymptomatic Men	4.69 (4.59,4.77)	3195 (2360,4314)	4.77 (6.05,6.1)	6791 (6235,7203)	4.72 (4.67,4.79)	7533 (6742,8187)	0.06 (0.02,0.13)	3760 (2931,4299)	62754 (21619,233719)
	80 year old Asymptomatic Women	5.52 (5.42,5.59)	3261 (2490,4340)	5.59 (7.1,7.15)	6897 (6386,7331)	5.55 (5.48,5.62)	7660 (6837,8361)	0.05 (0.01,0.14)	3814 (2881,4365)	73726 (19153,435377)
	65 year old Symptomatic Men	9.51 (9.01,9.84)	12545 (9041,17756)	9.83 (13.32,13.45)	13144 (11094,15199)	9.7 (9.39,9.97)	15443 (12255,18913)	0.21 (0.05,0.46)	1782 (-892,3519)	8615 (-1993,66715)
	65 year old Symptomatic Women	11.33 (10.77,11.68)	13265 (9279,18874)	11.66 (15.85,15.99)	13721 (11528,15826)	11.52 (11.15,11.8)	16177 (12812,20069)	0.21 (0.03,0.48)	1833 (-1194,3742)	8802 (-3216,87224)

	70 year old Symptomatic Men	7.16 (6.86,7.35)	8708 (6260,12124)	7.34 (10.07,10.15)	10586 (9158,11770)	7.26 (7.05,7.42)	12320 (10015,14572)	0.13 (0.03,0.33)	2558 (-21,3906)	19171 (-636,126323)
	70 year old Symptomatic Women	8.6 (8.31,8.82)	9263 (6610,12634)	8.81 (12.12,12.21)	11052 (9559,12381)	8.71 (8.48,8.9)	12909 (10457,15376)	0.14 (0.02,0.34)	2586 (-4,3937)	19103 (-671,160684)
	75 year old Symptomatic Men	5.02 (4.82,5.16)	6210 (4304,8814)	5.14 (7.18,7.23)	8878 (7716,9825)	5.08 (4.94,5.19)	10195 (8488,11827)	0.09 (0.01,0.23)	3033 (1088,4124)	33370 (3909,197170)
	75 year old Symptomatic Women	6.1 (5.88,6.25)	6557 (4558,9342)	6.23 (8.73,8.79)	9195 (7999,10218)	6.16 (6.01,6.28)	10597 (8751,12379)	0.09 (0.01,0.23)	3067 (1152,4099)	33475 (2692,247961)
	80 year old Symptomatic Men	3.29 (3.19,3.36)	3776 (2578,5500)	3.34 (4.79,4.82)	7285 (6551,7823)	3.31 (3.24,3.37)	8225 (7088,9297)	0.05 (0,0.13)	3671 (2387,4445)	80537 (-198588,645249)
	80 year old Symptomatic Women	4.03 (3.91,4.11)	3969 (2804,5796)	4.08 (5.86,5.89)	7483 (6762,8095)	4.05 (3.97,4.12)	8477 (7320,9498)	0.04 (0,0.13)	3702 (2460,4397)	83976 (-354748,588655)
Fatalities in major strokes = 45% (base case: 32.35%)	**65 year old Asymptomatic Men**	12.16 (11.65,12.53)	8658 (6463,11443)	12.63 (14.95,15.24)	10370 (9154,11320)	12.45 (12.11,12.75)	11994 (10105,13648)	0.28 (0.09,0.56)	2613 (924,3769)	9235 (1807,38403)
	65 year old Asymptomatic Women	14.04 (13.57,14.43)	8928 (6607,11874)	14.49 (17.23,17.52)	10635 (9476,11615)	14.31 (13.98,14.61)	12322 (10339,14177)	0.25 (0.09,0.58)	2704 (815,3706)	10608 (1696,40271)
	70 year old Asymptomatic Men	9.37 (9.07,9.61)	6112 (4596,7911)	9.66 (11.61,11.81)	8719 (7891,9404)	9.54 (9.32,9.73)	9948 (8676,11166)	0.19 (0.06,0.39)	3136 (1845,3975)	16320 (4898,62103)
	70 year old Asymptomatic Women	10.9 (10.59,11.16)	6338 (4780,8362)	11.18 (13.51,13.71)	8949 (8022,9633)	11.06 (10.83,11.26)	10229 (8831,11546)	0.17 (0.04,0.37)	3198 (1915,4038)	18322 (5551,91158)
	75 year old Asymptomatic Men	6.78 (6.56,6.95)	4399 (3232,5825)	6.97 (8.55,8.69)	7572 (6926,8129)	6.89 (6.75,7.02)	8509 (7532,9431)	0.14 (0.04,0.28)	3466 (2467,4171)	25357 (9176,92158)
	75 year old Asymptomatic Women	7.96 (7.74,8.13)	4540 (3385,6004)	8.14 (10.03,10.17)	7736 (7029,8271)	8.06 (7.91,8.2)	8707 (7651,9522)	0.12 (0.04,0.28)	3521 (2413,4150)	28428 (8739,102021)

	80 year old Asymptomatic Men	4.64 (4.51,4.74)	2767 (2054,3631)	4.74 (5.97,6.05)	6516 (5982,6847)	4.69 (4.6,4.77)	7196 (6523,7739)	0.07 (0.02,0.17)	3887 (3104,4354)	53117 (18027,194326)
	80 year old Asymptomatic Women	5.47 (5.35,5.57)	2839 (2132,3782)	5.56 (7.02,7.1)	6621 (6119,6978)	5.51 (5.43,5.59)	7321 (6642,7837)	0.06 (0.01,0.15)	3931 (3206,4421)	61068 (19199,353497)
	65 year old Symptomatic Men	9.14 (8.47,9.58)	9898 (7333,13871)	9.59 (12.71,13.09)	11477 (9812,12930)	9.42 (8.91,9.75)	13451 (11052,15894)	0.3 (0.06,0.68)	2469 (129,3814)	8241 (155,52788)
	65 year old Symptomatic Women	10.93 (10.21,11.39)	10506 (7697,14367)	11.41 (15.21,15.61)	11981 (10105,13468)	11.21 (10.7,11.59)	14092 (11294,16572)	0.3 (0.06,0.67)	2512 (318,3690)	8334 (429,51485)
	70 year old Symptomatic Men	6.93 (6.55,7.22)	6918 (4980,9481)	7.2 (9.69,9.93)	9454 (8276,10288)	7.08 (6.78,7.32)	10960 (9082,12531)	0.19 (0.03,0.44)	3051 (1360,4074)	15801 (2454,99815)
	70 year old Symptomatic Women	8.36 (7.9,8.68)	7387 (5346,10131)	8.65 (11.7,11.96)	9861 (8507,10867)	8.52 (8.21,8.76)	11473 (9427,13190)	0.2 (0.03,0.49)	3078 (1223,4022)	15687 (1626,92717)
	75 year old Symptomatic Men	4.87 (4.6,5.06)	4953 (3522,6839)	5.04 (6.93,7.09)	8081 (7213,8773)	4.97 (4.78,5.12)	9234 (7840,10423)	0.13 (0.02,0.32)	3406 (1936,4155)	25994 (5349,153805)
	75 year old Symptomatic Women	5.95 (5.66,6.15)	5251 (3802,7163)	6.13 (8.45,8.63)	8361 (7377,8969)	6.04 (5.84,6.2)	9590 (8059,10570)	0.13 (0.01,0.33)	3437 (2033,4187)	25906 (4580,193195)
	80 year old Symptomatic Men	3.21 (3.08,3.32)	3033 (2155,4170)	3.3 (4.66,4.75)	6802 (6173,7205)	3.25 (3.16,3.34)	7639 (6712,8321)	0.07 (0,0.18)	3893 (2883,4448)	59070 (10451,448465)
	80 year old Symptomatic Women	3.95 (3.8,4.06)	3203 (2306,4324)	4.03 (5.71,5.81)	6980 (6295,7382)	3.99 (3.87,4.07)	7864 (6846,8682)	0.06 (0,0.18)	3921 (2843,4473)	60482 (4304,540783)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.16: Deterministic sensitivity analyses (proportional increase in non-stroke vascular mortality) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
x1 increase in non-stroke vasc.[3] Mortality (base case: x2.45)	65 year old Asymptomatic Men	12.53 (12.16,12.82)	10329 (7672,13819)	12.86 (15.35,15.54)	11376 (9938,12534)	12.74 (12.43,12.95)	13242 (11033,15525)	0.2 (0.06,0.42)	2228 (395,3533)	10955 (1050,53431)
	65 year old Asymptomatic Women	14.37 (13.88,14.66)	10419 (7620,13971)	14.69 (17.6,17.79)	11536 (10044,12816)	14.56 (14.25,14.8)	13440 (10980,15888)	0.19 (0.05,0.41)	2377 (491,3620)	12654 (1093,66752)
	70 year old Asymptomatic Men	9.62 (9.38,9.81)	7284 (5381,9646)	9.82 (11.9,12.02)	9430 (8360,10271)	9.74 (9.56,9.88)	10841 (9245,12430)	0.13 (0.03,0.31)	2844 (1225,3812)	21327 (4394,127014)
	70 year old Asymptomatic Women	11.13 (10.86,11.34)	7402 (5406,9808)	11.32 (13.77,13.89)	9601 (8514,10437)	11.24 (11.07,11.4)	11047 (9394,12654)	0.12 (0.03,0.29)	2946 (1212,3894)	23782 (4410,123828)
	75 year old Asymptomatic Men	6.96 (6.77,7.08)	5236 (3906,7002)	7.08 (8.76,8.84)	8085 (7313,8714)	7.03 (6.9,7.13)	9158 (7953,10219)	0.09 (0.02,0.22)	3237 (1935,4046)	35190 (8651,173499)
	75 year old Asymptomatic Women	8.12 (7.96,8.25)	5304 (3859,7229)	8.24 (10.22,10.3)	8209 (7420,8757)	8.19 (8.06,8.29)	9308 (8056,10411)	0.09 (0.01,0.21)	3323 (2065,4110)	39065 (9573,287938)
	80 year old Asymptomatic Men	4.74 (4.65,4.81)	3260 (2408,4223)	4.8 (6.1,6.14)	6830 (6269,7241)	4.77 (4.71,4.82)	7601 (6823,8326)	0.05 (0.01,0.12)	3750 (2879,4326)	78991 (22666,477213)
	80 year old Asymptomatic Women	5.56 (5.45,5.63)	3291 (2454,4352)	5.62 (7.13,7.18)	6914 (6314,7316)	5.59 (5.51,5.65)	7700 (6815,8371)	0.04 (0,0.11)	3813 (2909,4322)	90464 (16614,666554)
	65 year old Symptomatic Men	10.55 (9.87,11.05)	13399 (9776,18565)	11.06 (14.92,15.29)	13794 (11528,15781)	10.86 (10.39,11.27)	16191 (12744,19512)	0.32 (0.07,0.7)	1742 (-976,3413)	5405 (-1797,36675)
	65 year old Symptomatic Women	12.17 (11.48,12.72)	13548 (9828,18710)	12.68 (17.16,17.53)	13979 (11608,15969)	12.48 (11.98,12.86)	16468 (13099,20058)	0.31 (0.08,0.71)	1904 (-924,3494)	6179 (-1521,35936)

	70 year old Symptomatic Men	8.17 (7.71,8.5)	9616 (6630,13290)	8.49 (11.63,11.86)	11231 (9560,12602)	8.36 (7.99,8.64)	13076 (10393,15616)	0.22 (0.04,0.5)	2436 (212,3684)	11069 (179,75586)
	70 year old Symptomatic Women	9.5 (9.04,9.84)	9766 (6957,13528)	9.82 (13.49,13.72)	11425 (9725,12732)	9.68 (9.3,9.95)	13346 (10780,15718)	0.21 (0.04,0.49)	2557 (250,3772)	12087 (314,79299)
	75 year old Symptomatic Men	5.93 (5.61,6.14)	7046 (5113,9669)	6.14 (8.57,8.73)	9452 (8242,10454)	6.05 (5.82,6.22)	10877 (9020,12529)	0.16 (0.03,0.35)	2876 (1093,3942)	18297 (3035,100476)
	75 year old Symptomatic Women	6.96 (6.64,7.19)	7112 (4912,9901)	7.17 (10.02,10.18)	9586 (8348,10707)	7.07 (6.84,7.25)	11064 (9209,12667)	0.15 (0.01,0.39)	2986 (1008,4060)	19841 (453,119660)
	80 year old Symptomatic Men	4.07 (3.89,4.2)	4481 (3120,6230)	4.18 (5.98,6.07)	7754 (6929,8393)	4.13 (4.01,4.23)	8789 (7563,9832)	0.09 (0.01,0.21)	3499 (2209,4241)	40704 (9816,255118)
	80 year old Symptomatic Women	4.8 (4.63,4.93)	4493 (3179,6289)	4.91 (7.02,7.11)	7839 (6980,8431)	4.85 (4.73,4.95)	8907 (7659,9894)	0.08 (0.01,0.21)	3587 (2164,4311)	44770 (7371,288893)
x1.5 increase in non-stroke vasc. Mortality (base case: x2.45)	**65 year old Asymptomatic Men**	12.43 (12.03,12.74)	9924 (7257,13185)	12.8 (15.25,15.45)	11133 (9761,12326)	12.66 (12.34,12.91)	12937 (10747,15180)	0.22 (0.08,0.44)	2311 (322,3534)	10317 (516,42068)
	65 year old Asymptomatic Women	14.28 (13.84,14.61)	10089 (7407,13576)	14.63 (17.51,17.71)	11338 (9878,12524)	14.5 (14.21,14.75)	13191 (10898,15544)	0.2 (0.04,0.43)	2442 (593,3680)	11968 (1311,74683)
	70 year old Asymptomatic Men	9.55 (9.26,9.76)	6993 (5115,9255)	9.77 (11.82,11.95)	9255 (8284,10031)	9.68 (9.5,9.84)	10617 (9100,12207)	0.15 (0.05,0.32)	2911 (1380,3883)	19439 (4254,72905)
	70 year old Asymptomatic Women	11.07 (10.78,11.27)	7158 (5341,9507)	11.28 (13.71,13.84)	9453 (8443,10286)	11.19 (11,11.35)	10858 (9278,12288)	0.14 (0.03,0.31)	3000 (1430,3888)	21864 (4495,111215)
	75 year old Asymptomatic Men	6.9 (6.72,7.04)	5026 (3714,6581)	7.05 (8.71,8.79)	7957 (7190,8542)	6.99 (6.86,7.09)	8993 (7911,10017)	0.11 (0.02,0.23)	3291 (2059,4094)	31327 (9249,177111)
	75 year old Asymptomatic Women	8.08 (7.89,8.21)	5125 (3850,6776)	8.21 (10.17,10.26)	8100 (7344,8704)	8.15 (8.01,8.26)	9165 (8006,10203)	0.1 (0.01,0.23)	3366 (2088,4186)	35131 (7338,172556)

	80 year old Asymptomatic Men	4.71 (4.61,4.78)	3139 (2343,4190)	4.78 (6.06,6.11)	6753 (6212,7141)	4.74 (4.68,4.81)	7499 (6715,8215)	0.06 (0.01,0.13)	3782 (2883,4329)	68495 (21104,310729)
	80 year old Asymptomatic Women	5.53 (5.43,5.61)	3187 (2398,4167)	5.6 (7.1,7.16)	6846 (6276,7176)	5.56 (5.49,5.63)	7610 (6788,8162)	0.05 (0,0.12)	3839 (3051,4358)	79085 (20364,654814)
	65 year old Symptomatic Men	10.07 (9.48,10.52)	12463 (8881,17043)	10.53 (14.17,14.5)	13159 (11010,14744)	10.35 (9.91,10.72)	15444 (12214,18321)	0.3 (0.05,0.66)	1910 (-769,3489)	6406 (-1634,51303)
	65 year old Symptomatic Women	11.76 (11.12,12.25)	12825 (9203,17073)	12.24 (16.53,16.86)	13492 (11428,15180)	12.05 (11.56,12.43)	15892 (12488,19104)	0.29 (0.05,0.64)	2026 (-758,3667)	6974 (-1444,59423)
	70 year old Symptomatic Men	7.73 (7.35,8.04)	8848 (6212,11967)	8.01 (10.94,11.15)	10716 (9098,11992)	7.89 (7.56,8.14)	12466 (10043,14763)	0.2 (0.03,0.45)	2594 (570,3913)	13008 (1159,103699)
	70 year old Symptomatic Women	9.1 (8.64,9.43)	9151 (6409,12562)	9.4 (12.87,13.09)	11014 (9448,12281)	9.27 (8.96,9.52)	12856 (10352,15078)	0.2 (0.03,0.44)	2676 (647,3867)	13682 (893,86037)
	75 year old Symptomatic Men	5.54 (5.26,5.73)	6425 (4587,9069)	5.73 (7.97,8.11)	9041 (7894,9951)	5.65 (5.45,5.8)	10385 (8656,11947)	0.14 (0.02,0.34)	3022 (1101,3981)	21599 (2845,129321)
	75 year old Symptomatic Women	6.6 (6.27,6.81)	6603 (4523,9455)	6.78 (9.47,9.62)	9247 (8091,10090)	6.7 (6.49,6.87)	10656 (8773,12395)	0.14 (0.02,0.34)	3099 (1343,4043)	22668 (2171,138467)
	80 year old Symptomatic Men	3.75 (3.59,3.87)	4029 (2821,5714)	3.84 (5.49,5.57)	7456 (6698,8035)	3.8 (3.67,3.88)	8429 (7303,9560)	0.07 (0.01,0.18)	3618 (2411,4288)	48707 (11660,433240)
	80 year old Symptomatic Women	4.49 (4.32,4.6)	4116 (2981,5739)	4.58 (6.55,6.62)	7587 (6803,8117)	4.53 (4.42,4.62)	8601 (7387,9547)	0.07 (0,0.2)	3681 (2359,4404)	52154 (-210122,434086)
x2 increase in non-stroke vasc. Mortality	**65 year old Asymptomatic Men**	12.34 (11.91,12.65)	9571 (7249,12884)	12.74 (15.15,15.38)	10921 (9501,12079)	12.59 (12.31,12.85)	12670 (10492,14770)	0.24 (0.07,0.48)	2386 (576,3649)	9840 (1258,51500)
	65 year old Asymptomatic Women	14.21 (13.78,14.55)	9794 (7215,13244)	14.59 (17.44,17.65)	11162 (9781,12277)	14.44 (14.17,14.71)	12970 (10883,15130)	0.22 (0.05,0.44)	2500 (698,3735)	11435 (1550,74365)

(base case: x2.45)	**70 year old Asymptomatic Men**	9.48 (9.19,9.71)	6740 (4907,8908)	9.73 (11.75,11.9)	9102 (8197,9895)	9.63 (9.43,9.81)	10422 (8945,11799)	0.16 (0.05,0.34)	2970 (1465,3901)	18083 (4671,76663)
	70 year old Asymptomatic Women	11.01 (10.73,11.22)	6941 (5264,9191)	11.25 (13.64,13.79)	9322 (8359,10151)	11.15 (10.95,11.31)	10690 (9181,12179)	0.15 (0.04,0.32)	3048 (1548,3951)	20431 (4639,98227)
	75 year old Asymptomatic Men	6.86 (6.65,7.01)	4844 (3534,6426)	7.02 (8.66,8.76)	7846 (7132,8447)	6.95 (6.82,7.07)	8850 (7757,9912)	0.12 (0.03,0.24)	3339 (2231,4145)	28640 (9917,142879)
	75 year old Asymptomatic Women	8.04 (7.82,8.19)	4967 (3674,6507)	8.19 (10.13,10.23)	8003 (7273,8505)	8.12 (7.99,8.25)	9039 (7849,9884)	0.11 (0.03,0.24)	3405 (2162,4114)	32283 (9198,126699)
	80 year old Asymptomatic Men	4.68 (4.58,4.76)	3032 (2298,3941)	4.76 (6.03,6.09)	6686 (6165,7057)	4.72 (4.65,4.79)	7410 (6638,8047)	0.06 (0.01,0.14)	3811 (2981,4388)	61396 (20157,365436)
	80 year old Asymptomatic Women	5.51 (5.39,5.6)	3093 (2301,4128)	5.58 (7.08,7.13)	6786 (6255,7182)	5.54 (5.46,5.61)	7529 (6805,8176)	0.05 (0.01,0.13)	3862 (3122,4384)	71119 (23241,475041)
	65 year old Symptomatic Men	9.64 (9.04,10.08)	11656 (8233,16206)	10.07 (13.52,13.81)	12613 (10546,14378)	9.9 (9.48,10.23)	14801 (11684,17896)	0.28 (0.06,0.58)	2059 (-345,3512)	7428 (-741,49067)
	65 year old Symptomatic Women	11.4 (10.8,11.86)	12187 (8710,16650)	11.84 (15.95,16.27)	13063 (10987,14802)	11.66 (11.25,12.02)	15383 (12272,18571)	0.27 (0.05,0.61)	2135 (-510,3615)	7772 (-1124,62104)
	70 year old Symptomatic Men	7.34 (6.94,7.59)	8190 (5995,11128)	7.6 (10.33,10.51)	10277 (8976,11384)	7.49 (7.19,7.71)	11944 (9672,13996)	0.18 (0.03,0.41)	2732 (768,3898)	15036 (838,82431)
	70 year old Symptomatic Women	8.75 (8.32,9.03)	8612 (6180,11806)	9.02 (12.31,12.53)	10653 (9157,11679)	8.9 (8.61,9.14)	12425 (10065,14454)	0.18 (0.03,0.44)	2783 (602,3910)	15322 (1087,94720)
	75 year old Symptomatic Men	5.2 (4.95,5.38)	5896 (4236,8227)	5.37 (7.45,7.57)	8690 (7726,9520)	5.3 (5.1,5.43)	9967 (8390,11530)	0.13 (0.02,0.3)	3148 (1550,4017)	25123 (5279,185390)
	75 year old Symptomatic Women	6.27 (6.01,6.47)	6158 (4367,8517)	6.44 (8.97,9.1)	8950 (7878,9793)	6.36 (6.17,6.51)	10300 (8578,11838)	0.12 (0.01,0.31)	3200 (1578,4183)	25646 (2580,153152)

	80 year old Symptomatic Men	3.47 (3.34,3.56)	3645 (2594,5039)	3.55 (5.06,5.13)	7203 (6504,7676)	3.51 (3.41,3.58)	8124 (7114,9028)	0.06 (0,0.16)	3719 (2567,4349)	57576 (13839,430374)
	80 year old Symptomatic Women	4.21 (4.06,4.31)	3787 (2755,5268)	4.29 (6.12,6.19)	7367 (6690,7917)	4.24 (4.14,4.33)	8335 (7205,9203)	0.06 (-0.01,0.17)	3763 (2509,4452)	60299 (-291184,413341)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

[3] *i.e. no increased non-stroke vascular mortality risks in patients following stroke*

Appendix Table 5.17: Deterministic sensitivity analyses (decrease in post-procedural stroke risks) results

Undiscounted QALYs and lifetime costs; Discounted incremental results

Change in model Inputs	Patient group	MT		CEA+MT		CAS+MT		CEA+MT vs MT		
		QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	QALY[1]	Cost (£)[1]	Inc QALYs[2]	Inc Cost (£)[2]	ICER (£)[2]
Post-procedural stroke rates (reduced by 10%): Asymp: major (0.38%); minor (0.31%) Symp: major (0.88%); minor (0.41%)	65 year old Asymptomatic Men	12.37 (12.03,12.61)	8613 (6729,10879)	12.76 (15.22,15.27)	10359 (9516,10942)	12.6 (12.34,12.81)	11994 (10421,13603)	0.23 (0.09,0.46)	2653 (988,3687)	11604 (2335,39743)
	65 year old Asymptomatic Women	14.25 (13.91,14.51)	8860 (6802,11285)	14.61 (17.5,17.56)	10623 (9710,11296)	14.46 (14.24,14.66)	12319 (10617,13673)	0.2 (0.06,0.42)	2758 (1098,3776)	13579 (2933,62892)
	70 year old Asymptomatic Men	9.5 (9.27,9.66)	6057 (4852,7856)	9.74 (11.79,11.83)	8709 (8098,9138)	9.64 (9.49,9.78)	9943 (8774,10865)	0.15 (0.05,0.31)	3180 (1880,3927)	20536 (6015,69357)
	70 year old Asymptomatic Women	11.03 (10.79,11.2)	6270 (4993,7987)	11.26 (13.68,13.73)	8940 (8287,9379)	11.16 (11.01,11.3)	10224 (8997,11218)	0.14 (0.03,0.29)	3251 (2017,4094)	23476 (7152,112863)
	75 year old Asymptomatic Men	6.87 (6.71,6.98)	4346 (3435,5590)	7.02 (8.68,8.71)	7563 (7084,7910)	6.95 (6.86,7.05)	8503 (7650,9254)	0.11 (0.04,0.23)	3507 (2551,4207)	31887 (11504,102357)
	75 year old Asymptomatic Women	8.05 (7.89,8.16)	4480 (3603,5729)	8.19 (10.15,10.19)	7728 (7196,8063)	8.12 (8.02,8.22)	8702 (7803,9414)	0.1 (0.02,0.22)	3568 (2474,4214)	36435 (11954,163415)
	80 year old Asymptomatic Men	4.69 (4.6,4.75)	2725 (2192,3477)	4.76 (6.04,6.06)	6512 (6131,6784)	4.72 (4.66,4.78)	7194 (6595,7672)	0.06 (0.01,0.13)	3922 (3192,4408)	67775 (24337,332867)
	80 year old Asymptomatic Women	5.52 (5.43,5.58)	2795 (2244,3557)	5.58 (7.09,7.11)	6619 (6197,6886)	5.54 (5.49,5.6)	7320 (6666,7783)	0.05 (0.01,0.13)	3970 (3188,4384)	80095 (22610,392376)
	65 year old Symptomatic Men	9.4 (8.99,9.68)	10231 (7946,13451)	9.75 (13.14,13.18)	11693 (10522,12538)	9.61 (9.31,9.86)	13731 (11337,15873)	0.23 (0.04,0.5)	2407 (220,3714)	10319 (146,65769)
	65 year old Symptomatic Women	11.2 (10.75,11.55)	10831 (8288,13910)	11.58 (15.65,15.7)	12205 (10916,13011)	11.42 (11.08,11.68)	14383 (11901,16475)	0.23 (0.04,0.54)	2465 (250,3754)	10580 (-30,71741)

	70 year old Symptomatic Men	7.09 (6.83,7.27)	7107 (5553,9109)	7.3 (9.95,9.98)	9594 (8731,10111)	7.2 (7.01,7.36)	11141 (9533,12431)	0.15 (0.02,0.35)	3026 (1257,4032)	20363 (2847,163801)
	70 year old Symptomatic Women	8.53 (8.23,8.74)	7575 (5854,9765)	8.76 (11.98,12.02)	10009 (9062,10567)	8.65 (8.47,8.83)	11665 (9837,12932)	0.15 (0.02,0.35)	3062 (1304,4047)	20465 (3136,145537)
	75 year old Symptomatic Men	4.98 (4.8,5.1)	5065 (3842,6793)	5.11 (7.1,7.12)	8174 (7569,8529)	5.04 (4.93,5.14)	9355 (8161,10254)	0.1 (0.01,0.23)	3399 (2035,4193)	33931 (6594,231373)
	75 year old Symptomatic Women	6.06 (5.86,6.19)	5362 (4191,7024)	6.19 (8.64,8.67)	8461 (7739,8859)	6.12 (6,6.24)	9719 (8328,10732)	0.1 (0,0.25)	3437 (2023,4211)	34279 (5448,210380)
	80 year old Symptomatic Men	3.27 (3.17,3.33)	3084 (2364,4118)	3.33 (4.75,4.76)	6859 (6361,7139)	3.29 (3.23,3.35)	7712 (6873,8285)	0.05 (0,0.13)	3902 (2916,4419)	79185 (8337,541514)
	80 year old Symptomatic Women	4.01 (3.91,4.08)	3253 (2559,4306)	4.07 (5.81,5.83)	7041 (6505,7324)	4.03 (3.96,4.09)	7944 (7058,8546)	0.05 (0,0.13)	3934 (2921,4429)	83106 (-282501,654816)
Post-procedural stroke rates (reduced by 20%): Asymp: major (0.34%); minor (0.28%) Symp: major (0.78%); minor (0.37%)	**65 year old Asymptomatic Men**	12.48 (12.16,12.71)	7914 (6214,10325)	12.82 (15.27,15.32)	9959 (9133,10523)	12.68 (12.46,12.87)	11519 (10008,12957)	0.2 (0.07,0.39)	2871 (1285,3761)	14427 (3440,53857)
	65 year old Asymptomatic Women	14.35 (14.06,14.57)	8143 (6456,10420)	14.67 (17.54,17.6)	10221 (9365,10796)	14.53 (14.33,14.72)	11838 (10255,13147)	0.17 (0.06,0.38)	2975 (1494,3823)	17028 (4315,58695)
	70 year old Asymptomatic Men	9.57 (9.34,9.73)	5561 (4482,7135)	9.78 (11.82,11.86)	8432 (7851,8881)	9.68 (9.54,9.81)	9612 (8499,10558)	0.13 (0.04,0.28)	3348 (2212,4019)	25145 (7918,95913)
	70 year old Asymptomatic Women	11.1 (10.88,11.25)	5762 (4636,7467)	11.3 (13.71,13.76)	8662 (8044,9071)	11.2 (11.06,11.33)	9889 (8788,10819)	0.12 (0.03,0.26)	3420 (2178,4122)	29106 (7688,124635)
	75 year old Asymptomatic Men	6.92 (6.77,7.02)	3986 (3159,5049)	7.05 (8.7,8.73)	7365 (6878,7686)	6.98 (6.9,7.08)	8265 (7406,8931)	0.09 (0.03,0.21)	3641 (2690,4241)	38833 (12521,141355)
	75 year old Asymptomatic Women	8.1 (7.97,8.2)	4114 (3265,5108)	8.22 (10.17,10.21)	7531 (7038,7868)	8.15 (8.06,8.25)	8463 (7599,9107)	0.08 (0.02,0.19)	3702 (2758,4269)	45051 (14201,218974)

	80 year old Asymptomatic Men	4.71 (4.63,4.77)	2499 (1957,3138)	4.78 (6.05,6.07)	6391 (6003,6678)	4.74 (4.69,4.8)	7047 (6479,7478)	0.05 (0.01,0.12)	4013 (3360,4450)	83613 (27899,446690)
	80 year old Asymptomatic Women	5.54 (5.47,5.6)	2569 (2068,3257)	5.6 (7.1,7.12)	6499 (6087,6774)	5.56 (5.5,5.62)	7175 (6584,7645)	0.04 (0,0.11)	4060 (3317,4499)	101594 (24836,683690)
	65 year old Symptomatic Men	9.5 (9.09,9.78)	9406 (7160,12461)	9.81 (13.18,13.22)	11190 (10096,11850)	9.68 (9.43,9.91)	13151 (10861,14676)	0.2 (0.04,0.51)	2652 (214,3800)	12947 (217,76263)
	65 year old Symptomatic Women	11.31 (10.85,11.61)	9953 (7692,13153)	11.64 (15.7,15.75)	11681 (10459,12484)	11.49 (11.18,11.74)	13774 (11446,15845)	0.2 (0.02,0.47)	2721 (721,3844)	13419 (980,99346)
	70 year old Symptomatic Men	7.15 (6.91,7.34)	6518 (5019,8433)	7.34 (9.98,10.01)	9247 (8388,9717)	7.25 (7.07,7.4)	10736 (9071,12004)	0.13 (0.01,0.32)	3220 (1518,4197)	25047 (3614,200069)
	70 year old Symptomatic Women	8.6 (8.32,8.79)	6948 (5397,9181)	8.8 (12.01,12.05)	9646 (8735,10126)	8.7 (8.49,8.85)	11240 (9528,12532)	0.13 (0,0.32)	3264 (1551,4101)	25494 (-70652,163896)
	75 year old Symptomatic Men	5.02 (4.86,5.12)	4632 (3631,6069)	5.13 (7.12,7.14)	7927 (7300,8250)	5.07 (4.97,5.16)	9064 (7877,9822)	0.09 (0,0.22)	3556 (2178,4231)	41447 (7545,284464)
	75 year old Symptomatic Women	6.1 (5.94,6.22)	4907 (3829,6538)	6.22 (8.66,8.69)	8204 (7528,8573)	6.15 (6.03,6.26)	9417 (8172,10335)	0.08 (-0.01,0.23)	3599 (2204,4324)	42473 (-299010,213104)
	80 year old Symptomatic Men	3.29 (3.2,3.35)	2814 (2194,3735)	3.34 (4.76,4.77)	6710 (6226,6981)	3.31 (3.25,3.36)	7535 (6756,8090)	0.04 (-0.01,0.12)	4009 (3095,4505)	97659 (-322258,734451)
	80 year old Symptomatic Women	4.03 (3.94,4.09)	2974 (2322,3936)	4.08 (5.82,5.84)	6887 (6371,7152)	4.04 (3.97,4.1)	7761 (6887,8332)	0.04 (-0.01,0.12)	4044 (3087,4534)	105207 (-651063,895933)

Symp: Symptomatic; Asymp: Asymptomatic; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; MT: Medical Therapy; QALY: Quality Adjusted Life Years

[1]*QALYs and costs are undiscounted.*

[2]*Incremental results, including ICERs, have been presented using discounted QALYs and lifetime costs*

Appendix Table 5.18: Expected value of perfect information per patient

Ceiling ratio (£)	65 year old Asymp Men (£)	65 year old Asymp Women (£)	70 year old Asymp Men (£)	70 year old Asymp Women (£)	75 year old Asymp Men (£)	75 year old Asymp Women (£)	80 year old Asymp Men (£)	80 year old Asymp Women (£)	65 year old Symp Men (£)	65 year old Symp Women (£)	70 year old Symp Men (£)	70 year old Symp Women (£)	75 year old Symp Men (£)	75 year old Symp Women (£)	80 year old Symp Men (£)	80 year old Symp Women (£)
0	2	1	-	-	-	-	-	-	15	31	1	2	-	-	-	-
1000	10	6	-	-	-	-	-	-	51	71	4	5	0	0	-	-
2000	29	18	1	0	-	-	-	-	115	135	10	11	0	1	-	-
3000	65	44	1	2	-	-	-	-	204	225	23	23	1	2	-	-
4000	120	88	4	4	-	-	-	-	314	337	45	42	2	4	-	-
5000	200	148	14	9	0	0	-	-	448	474	75	72	5	9	-	-
6000	308	232	32	18	1	1	-	-	601	636	115	112	10	15	-	-
7000	441	340	59	33	2	3	-	-	774	789	169	164	18	25	-	0
8000	600	468	97	55	6	7	-	-	701	702	234	229	27	38	-	0
9000	574	611	146	87	12	14	-	-	629	627	311	305	40	55	-	1
10000	492	637	207	130	21	23	-	-	567	563	401	388	57	78	0	2
11000	424	561	279	183	35	34	-	-	515	509	502	481	81	106	0	4
12000	368	497	363	246	53	49	-	-	471	463	611	582	110	141	1	5
13000	322	441	457	319	78	67	0	-	434	425	727	690	144	180	1	8
14000	284	392	563	401	107	89	0	-	403	393	849	806	182	224	2	11

15000	252	349	680	489	142	115	1	-	376	367	798	884	225	274	3	16
16000	225	312	624	587	183	146	3	0	352	343	748	830	273	329	6	21
17000	201	279	564	693	231	182	5	1	331	323	704	782	325	390	9	27
18000	180	251	512	642	284	222	7	2	314	306	665	738	381	455	14	33
19000	163	227	466	588	343	268	11	3	299	292	630	698	442	524	19	39
20000	**149**	**207**	**425**	**541**	**407**	**318**	**15**	**6**	**285**	**280**	**597**	**662**	**507**	**597**	**26**	**46**
21000	138	189	388	499	477	373	20	8	275	269	566	629	578	673	34	55
22000	129	175	355	461	552	432	26	12	266	259	539	599	651	753	43	64
23000	121	162	325	427	632	496	34	16	258	251	515	571	727	835	53	74
24000	114	151	299	396	715	564	42	21	251	245	493	546	805	889	64	87
25000	108	141	276	368	694	637	51	26	245	239	475	522	886	849	77	100
26000	103	133	255	342	649	715	62	33	240	234	458	500	871	812	90	115
27000	98	125	236	320	607	730	74	40	236	230	443	480	835	778	104	131
28000	94	118	219	299	569	688	88	49	232	227	429	461	801	745	120	148
29000	91	113	203	281	535	650	105	59	229	224	416	445	768	716	136	166
30000	**88**	**108**	**190**	**265**	**503**	**615**	**123**	**70**	**226**	**222**	**404**	**430**	**739**	**689**	**154**	**185**
31000	85	104	178	251	474	581	144	83	224	221	393	416	711	664	173	206
32000	83	100	167	239	448	551	166	97	222	220	383	403	685	640	193	228

33000	81	97	157	228	423	523	190	112	221	219	374	392	662	619	214	251
34000	79	94	148	219	400	497	215	127	219	219	365	381	640	599	237	276
35000	78	91	140	210	379	473	242	145	218	218	357	371	619	580	261	301
36000	77	89	133	203	359	451	271	163	217	219	350	362	600	563	287	328
37000	76	87	126	195	340	431	303	182	217	219	342	354	582	547	314	356
38000	75	86	121	189	323	412	336	204	217	220	336	346	564	532	342	385
39000	75	84	116	183	307	394	372	227	217	221	330	340	549	518	371	415
40000	75	83	112	178	293	377	409	252	217	222	324	334	534	505	401	446
41000	75	82	108	173	279	362	448	277	218	222	319	328	520	492	432	479
42000	75	82	104	169	266	348	489	304	218	223	314	323	507	480	464	512
43000	75	82	101	165	253	334	531	332	219	225	310	318	494	469	496	546
44000	75	81	98	162	242	322	576	361	220	226	306	314	483	458	530	582
45000	76	81	95	158	231	310	621	392	221	228	302	310	472	449	564	618
46000	76	81	93	155	221	299	667	425	223	229	299	307	462	440	599	655
47000	76	81	90	153	212	289	715	459	224	231	296	304	453	432	635	693
48000	77	81	88	150	204	280	764	495	225	233	293	301	444	424	672	731
49000	78	81	86	148	196	272	787	531	226	235	290	298	435	417	711	771
50000	78	81	84	146	189	264	762	569	228	237	288	296	427	410	750	811

Symp: Symptomatic; Asymp: Asymptomatic

Appendix Table 5.19: Expected value of partial perfect information (EVPPI) per patient at willingness to pay-per-QALY of £ 20,000

Input parameters	65 year old Asymptomatic Men (£)	65 year old Asymptomatic Women (£)	70 year old Asymptomatic Men (£)	70 year old Asymptomatic Women (£)	75 year old Asymptomatic Men (£)	75 year old Asymptomatic Women (£)	80 year old Asymptomatic Men (£)	80 year old Asymptomatic Women (£)	65 year old Symptomatic Men (£)	65 year old Symptomatic Women (£)	70 year old Symptomatic Men (£)	70 year old Symptomatic Women (£)	75 year old Symptomatic Men (£)	75 year old Symptomatic Women (£)	80 year old Symptomatic Men (£)	80 year old Symptomatic Women (£)
Relative procedural stroke/death risks of CAS vs CEA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Relative post-procedural major and minor stroke risks of CAS+MT vs CEA+MT	40	47	0	0	0	0	0	0	65	68	0	0	0	0	0	0
CEA: procedural stroke/death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Absolute post-procedural major and minor stroke risks of CEA patients	0	0	48	36	62	93	0	0	0	0	45	29	59	106	0	0
Relative post-procedural major and minor stroke risks of CEA+MT vs MT alone	246	298	760	810	563	402	0	0	208	221	729	614	442	510	0	0

Appendix Table 5.20: : Summary of cost-effectiveness results in Morris et al(23)

Patient group	CAS+MT vs CEA+MT	
	Inc QALYs*	**Inc Cost (US$)***
Base Case	-0.01 (-0.117, 0.097)	736 (-353, 1826)
By Gender		
Men	-0.055 (-0.185, 0.076)	481 (-672, 1634)
Women	0.103 (-0.098, 0.304)	1123 (-1153, 3400)
By age		
Age >= 70	-0.061 (-0.219, 0.097)	1112 (-461, 2685)
Age <=70	0.057 (-0.094, 0.208)	204 (-1018, 1426)

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; QALY: Quality Adjusted Life Years; Inc: Incremental

**Inc Cost and Inc QALYs adjusted for potential confounders*

Appendix Table 5.21: Cost-effectiveness results (discounted) after limiting time-horizon of model to 5-years and sourcing relative post-procedural stroke risks from ICSS

Patient Group	CEA+MT		CAS+MT		CEA+MT vs CAS+MT	
	QALY	Cost	QALY	Cost	Inc QALYs	Inc Cost
65 year old Symptomatic Men	3.34 (3.22,3.46)	6342 (5842,6666)	3.32 (3.18,3.45)	7244 (6356,7956)	0.02 (-0.01,0.06)	-902 (-1708,-156)
65 year old Symptomatic Women	3.45 (3.32,3.57)	6187 (5668,6509)	3.43 (3.3,3.56)	7024 (6190,7675)	0.02 (-0.01,0.06)	-837 (-1511,-164)
75 year old Symptomatic Men	2.77 (2.67,2.88)	6345 (5825,6667)	2.75 (2.64,2.87)	7247 (6372,8088)	0.02 (-0.01,0.07)	-902 (-1763,-206)
75 year old Symptomatic Women	2.97 (2.86,3.09)	6230 (5713,6572)	2.95 (2.83,3.07)	7085 (6266,7855)	0.02 (-0.01,0.06)	-855 (-1663,-171)

CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; QALY: Quality Adjusted Life Years; Inc: Incremental

Appendix Table 5.22: Cost-effectiveness results (discounted) after setting procedural costs of CEA and CAS to zero

Patient Group	MT			CEA			CAS		
	LY	QALY	Cost	LY	QALY	Cost	LY	QALY	Cost
65 year old Asymptomatic Men	11.22 (11,11.41)	9.39 (9.06,9.67)	6532 (4644,8592)	11.42 (11.35,11.5)	9.64 (9.45,9.84)	4449 (3543,5136)	11.35 (11.19,11.48)	9.54 (9.29,9.79)	5473 (4024,6714)
65 year old Asymptomatic Women	12.6 (12.37,12.76)	10.52 (10.18,10.79)	6474 (4774,9028)	12.77 (12.7,12.84)	10.75 (10.56,10.96)	4494 (3621,5235)	12.7 (12.52,12.82)	10.65 (10.42,10.9)	5533 (4127,6881)
70 year old Asymptomatic Men	9.21 (9.03,9.34)	7.59 (7.33,7.8)	4927 (3629,6433)	11.78 (9.3,9.41)	7.77 (7.61,7.93)	3417 (2779,3889)	9.29 (9.17,9.4)	7.69 (7.49,7.88)	4208 (3127,5242)
70 year old Asymptomatic Women	10.47 (10.3,10.59)	8.61 (8.34,8.84)	4942 (3630,6493)	10.59 (10.54,10.65)	8.77 (8.6,8.95)	3501 (2811,3974)	10.54 (10.42,10.63)	8.69 (8.5,8.91)	4312 (3205,5241)
75 year old Asymptomatic Men	7.15 (7.01,7.24)	5.76 (5.57,5.92)	3812 (2819,5174)	7.25 (7.21,7.29)	5.89 (5.78,6.02)	2661 (2154,3040)	7.2 (7.12,7.28)	5.83 (5.69,5.99)	3268 (2409,4024)
75 year old Asymptomatic Women	8.23 (8.1,8.32)	6.62 (6.41,6.81)	3827 (2802,5099)	8.32 (8.28,8.36)	6.74 (6.6,6.88)	2737 (2231,3103)	8.27 (8.19,8.35)	6.68 (6.51,6.85)	3361 (2488,4041)
80 year old Asymptomatic Men	5.23 (5.15,5.29)	4.11 (3.97,4.22)	2530 (1881,3345)	5.29 (5.27,5.32)	4.17 (4.07,4.29)	1836 (1499,2083)	5.26 (5.21,5.31)	4.14 (4.03,4.26)	2251 (1672,2713)
80 year old Asymptomatic Women	6.07 (5.99,6.13)	4.77 (4.62,4.89)	2545 (1942,3408)	6.12 (6.1,6.15)	4.83 (4.72,4.95)	1899 (1555,2139)	6.09 (6.04,6.14)	4.79 (4.66,4.92)	2326 (1742,2781)
65 year old Symptomatic Men	9.98 (9.69,10.18)	7.33 (6.92,7.67)	7963 (5719,10848)	10.16 (10.06,10.25)	7.59 (7.39,7.81)	5613 (4321,6741)	10.1 (9.84,10.25)	7.48 (7.14,7.75)	6977 (4884,8850)
65 year old Symptomatic Women	11.53 (11.24,11.76)	8.47 (8.05,8.82)	8091 (5804,11324)	11.72 (11.61,11.81)	8.74 (8.51,8.96)	5788 (4450,6903)	11.65 (11.39,11.81)	8.62 (8.27,8.91)	7213 (5106,9391)
70 year old Symptomatic Men	8.01 (7.79,8.15)	5.81 (5.5,6.05)	5936 (4252,8224)	8.12 (8.05,8.18)	5.98 (5.81,6.14)	4250 (3250,5065)	8.08 (7.93,8.18)	5.91 (5.69,6.12)	5319 (3722,6784)
70 year old Symptomatic Women	9.39 (9.18,9.56)	6.82 (6.49,7.08)	6108 (4211,8428)	9.51 (9.44,9.58)	6.99 (6.8,7.18)	4450 (3419,5270)	9.47 (9.31,9.58)	6.9 (6.65,7.14)	5578 (3836,7081)
75 year old Symptomatic Men	6.01 (5.86,6.12)	4.28 (4.06,4.44)	4560 (3297,6307)	6.1 (6.05,6.14)	4.39 (4.26,4.52)	3280 (2587,3817)	6.06 (5.96,6.13)	4.34 (4.16,4.49)	4112 (2887,5146)
75 year old Symptomatic Women	7.17 (7.01,7.28)	5.1 (4.84,5.28)	4690 (3318,6586)	7.25 (7.2,7.3)	5.21 (5.06,5.36)	3442 (2653,4041)	7.22 (7.1,7.29)	5.15 (4.96,5.32)	4323 (2999,5537)
80 year old Symptomatic Men	4.22 (4.14,4.28)	2.93 (2.79,3.05)	2938 (2095,4102)	4.26 (4.23,4.28)	2.98 (2.88,3.09)	2209 (1721,2547)	4.24 (4.18,4.28)	2.95 (2.84,3.06)	2790 (1957,3430)
80 year old Symptomatic Women	5.09 (5,5.15)	3.53 (3.38,3.66)	3033 (2196,4311)	5.13 (5.1,5.15)	3.59 (3.48,3.7)	2333 (1789,2668)	5.11 (5.04,5.15)	3.55 (3.43,3.69)	2950 (2056,3684)

Appendix Table 5.23: **Cost-effectiveness results (discounted) after setting treatment effects of CAS vs CEA and CEA vs MT to 1**

Patient Group	MT			CEA			CAS		
	LY	QALY	Cost	LY	QALY	Cost	LY	QALY	Cost
65 year old Asymptomatic Men	11.48 (11.4,11.55)	9.71 (9.52,9.89)	4038 (3298,4769)	11.42 (11.35,11.5)	9.64 (9.46,9.83)	8977 (8044,9681)	11.42 (11.35,11.5)	9.64 (9.46,9.83)	9355 (8453,10085)
65 year old Asymptomatic Women	12.82 (12.75,12.89)	10.82 (10.64,11.03)	4032 (3294,4719)	12.77 (12.7,12.84)	10.75 (10.57,10.96)	9022 (8016,9655)	12.77 (12.7,12.84)	10.75 (10.57,10.96)	9398 (8448,10066)
70 year old Asymptomatic Men	9.4 (9.34,9.45)	7.82 (7.67,7.97)	3053 (2520,3619)	11.78 (9.3,9.41)	7.77 (7.62,7.92)	7945 (7225,8471)	9.35 (9.3,9.41)	7.77 (7.62,7.92)	8288 (7588,8831)
70 year old Asymptomatic Women	10.64 (10.59,10.69)	8.83 (8.67,9)	3094 (2573,3676)	10.59 (10.54,10.64)	8.77 (8.62,8.94)	8029 (7277,8585)	10.59 (10.54,10.64)	8.77 (8.62,8.94)	8371 (7657,8939)
75 year old Asymptomatic Men	7.29 (7.25,7.33)	5.93 (5.81,6.07)	2349 (1940,2750)	7.25 (7.21,7.29)	5.89 (5.76,6.02)	7189 (6570,7610)	7.25 (7.21,7.29)	5.89 (5.76,6.02)	7495 (6926,7893)
75 year old Asymptomatic Women	8.36 (8.32,8.4)	6.79 (6.63,6.93)	2390 (1987,2827)	8.32 (8.28,8.36)	6.74 (6.59,6.88)	7265 (6665,7693)	8.32 (8.28,8.36)	6.74 (6.59,6.88)	7571 (6971,8010)
80 year old Asymptomatic Men	5.32 (5.3,5.35)	4.21 (4.1,4.31)	1568 (1307,1831)	5.29 (5.27,5.32)	4.17 (4.06,4.28)	6364 (5923,6738)	5.29 (5.27,5.32)	4.17 (4.06,4.28)	6641 (6206,6951)
80 year old Asymptomatic Women	6.15 (6.13,6.18)	4.87 (4.74,4.99)	1604 (1355,1886)	6.12 (6.1,6.15)	4.83 (4.71,4.95)	6427 (5951,6787)	6.12 (6.1,6.15)	4.83 (4.71,4.95)	6703 (6282,7029)
65 year old Symptomatic Men	10.21 (10.11,10.3)	7.66 (7.42,7.88)	4963 (3814,6185)	10.16 (10.06,10.25)	7.59 (7.37,7.81)	10141 (8775,11298)	10.16 (10.06,10.25)	7.59 (7.37,7.81)	10519 (9161,11598)
65 year old Symptomatic Women	11.77 (11.67,11.86)	8.82 (8.59,9.04)	5055 (3982,6427)	11.72 (11.61,11.81)	8.74 (8.51,8.97)	10316 (8949,11583)	11.72 (11.61,11.81)	8.74 (8.51,8.97)	10691 (9339,11882)
70 year old Symptomatic Men	8.16 (8.09,8.22)	6.04 (5.86,6.22)	3674 (2868,4590)	8.12 (8.05,8.18)	5.98 (5.81,6.17)	8779 (7753,9545)	8.12 (8.05,8.18)	5.98 (5.81,6.17)	9122 (8102,9970)

70 year old Symptomatic Women	9.56 (9.49,9.62)	7.06 (6.88,7.23)	3802 (2999,4772)	9.51 (9.44,9.58)	6.99 (6.82,7.17)	8978 (7923,9820)	9.51 (9.44,9.58)	6.99 (6.82,7.17)	9320 (8305,10173)
75 year old Symptomatic Men	6.13 (6.08,6.17)	4.43 (4.3,4.56)	2789 (2179,3431)	6.1 (6.05,6.13)	4.39 (4.26,4.52)	7808 (6989,8429)	6.1 (6.05,6.13)	4.39 (4.26,4.52)	8115 (7342,8719)
75 year old Symptomatic Women	7.29 (7.24,7.33)	5.26 (5.12,5.42)	2892 (2286,3591)	7.25 (7.2,7.29)	5.21 (5.07,5.37)	7970 (7126,8586)	7.25 (7.2,7.29)	5.21 (5.07,5.37)	8277 (7403,8895)
80 year old Symptomatic Men	4.28 (4.25,4.3)	3.01 (2.91,3.11)	1788 (1422,2251)	4.26 (4.23,4.28)	2.98 (2.88,3.08)	6737 (6117,7158)	4.26 (4.23,4.28)	2.98 (2.88,3.09)	7014 (6439,7455)
80 year old Symptomatic Women	5.16 (5.12,5.18)	3.63 (3.51,3.74)	1868 (1491,2318)	5.13 (5.1,5.16)	3.59 (3.48,3.71)	6861 (6202,7314)	5.13 (5.1,5.16)	3.59 (3.48,3.71)	7138 (6557,7561)

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