SUPPLEMENTAL MATERIAL

- Methods and Search Results
- Supplemental Figure 1: PRISMA Diagram
- Table I: MEDLINE Search Terms
- Table II: Full List of Included Studies
- Table III: Baseline Characteristics of Selected Studies
- References

Supplemental Methods and Search Results:

Eligibility Criteria:

Studies related to asymptomatic carotid stenosis, carotid artery occlusions or near-occlusions, were excluded. Meta-analysis or systematic reviews reporting individual patient data from RCTs were also included, however observational studies, case series, and reports were not included due to the elevated risk of bias associated with non-randomized data. We had no restrictions on country of study, ethnicity, sex, socio-economic status of study populations, or healthcare location of research. We only included studies presented in the English and French language.

Information Sources and Search:

Supplementary searches included scanning the reference list of included studies and reviews identified through the primary search and ClinicalTrials.gov. The detailed search strategy using keywords and Medical Subject Headings (MeSH) terms is provided in Supplement Table I.

Study Selection:

Screening and full-text review was conducted using Covidence Systematic Review software (Covidence, Melbourne, Australia). A two-stage screening was performed by two independent reviewers (OB and BD). In stage one, both abstracts and titles were screened for potentially relevant articles. In stage two, full-text screening was performed using a screening form created a priori. A liberal accelerated method was utilized, requiring two reviewers to exclude a study. A pilot screening exercise was performed at both levels, with 100 records piloted for level 1 and 25 records piloted at level 2. Disputes were resolved by author, MS.

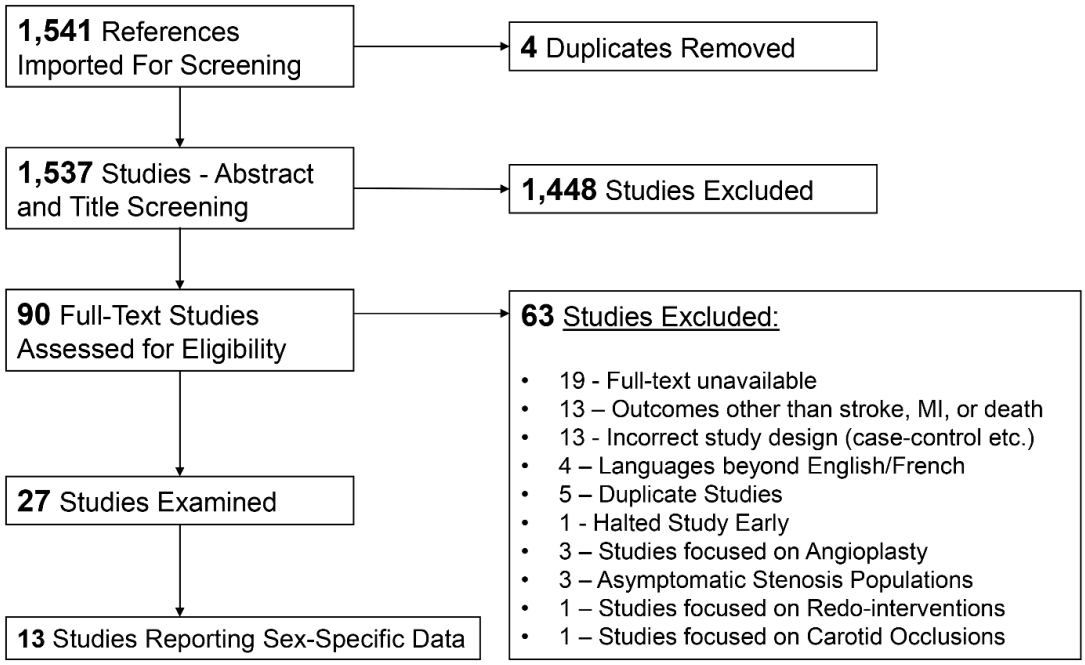
Data Charting Process and Selected Items:

Data extraction was conducted independently by each reviewer using an *a priori* collection form. We collected publication information, study population information, severity of ipsilateral carotid stenosis, type of ipsilateral event, treatment allocation, follow-up time, and outcome data.

Article Selection:

Among the 1,537 records retrieved, title and abstract screening narrowed our search to 90 articles that underwent full text screening. Reasons for exclusion included: assessment of different outcome, alternate study designs, and lack of full-text availability (i.e. published abstracts). All included studies were peer-reviewed original research contributions using clinical trial data.

Supplemental Figure 1: PRISMA Diagram



Supplemental Table I: Sample Search Strategy

1 Carotid Stenosis/ or carotid stenosis.kw.
2 (carotid adj3 (stenos$ or ulcer$ or plaque$ or narrow$ or obstruct$ or occlus$ or constrict$)).tw.
3 1 or 2
4 Endarterectomy, Carotid
5 endarterectom*.tw,kw.
6 STENTS/ or stent*.tw,kw.
7 carotid revascularization.tw,kw.
8 or/4-7
9 3 and 8
10 WOMEN
11 Sex Characteristics
12 sex factors
13 (female or women).tw
14 (sex or gender or women or female).ti.
15 (gender based or gender specific).tw.
16 ((sex or gender) adj2 (difference* or disparit*)).tw.
17 or/10-16
18 9 and 17
19 randomized controlled trial.pt.
20 controlled clinical trial.pt.
21 randomi?ed.ab.
22 placebo.ab.
23 clinical trials as topic.sh.
24 randomly.ab.
25 trial.ti.
26 groups.ab.
27 or/19-26
28 9 and 27
29 symptomatic.tw,kw.
30 28 and 29
31 18 and 27
32 30 or 31
33 limit 32 to yr="1990 -Current"
34 case reports.pt.
35 33 not 34
36 limit 35 to (english or french)

Supplemental Table II: Full List of Included Studies (n=27)

Study	Study Type	Interventions	Percent Stenosis	Outcome Assessed
North American Symptomatic Carotid Endarterectomy Trial Collaborators (NASCET)	RCT	CEA / BMT	70-99%	- 2-year longitudinal collection of death and stroke events[1] - 8-year longitudinal collection of stroke events (disabling, ipsilateral)[2] - 5-year risk of ipsilateral stroke stratified by percent stenosis (sex-specific data available)[3]
European Carotid Surgery Trialists' Collaborative Group (ECST)	RCT	CEA / BMT	70-99% 0-29%	- 30-day risk of death or disabling stroke[4] - 3-year longitudinal collection of death and stroke events[4] - 8-year longitudinal collection of death and stroke events[5] - Model of stroke-free life expectancy stratified by age and percent stenosis[6]
Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS)	RCT	CEA / CAS	70-99% 50-69% 0-49%	- 30-day risk of death or disabling stroke[7] - 3-year longitudinal collection of death and stroke[7] - Sex-specific 8-year longitudinal collection of stroke events (disabling, TIA) and/or death[8]
Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE)	RCT	CEA / CAS	> 50%* > 80%†	Death, stroke, myocardial infarction + Composite at 1 year[9]
Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE)	RCT	CEA / CAS	> 50%	- 30-day risk of death, stroke, bleeding, or composite[10] - Sex-specific 30 day risk of composite outcome[10]

Study	Study Type	Interventions	Percent Stenosis	Outcome Assessed
				- 2-year risk of ipsilateral ischemic stroke plus 30-day risk of stroke and death[11] - Sex-specific 2-year risk of ipsilateral ischemic stroke plus 30-day risk of stroke and death[11] - Study aimed at identifying risk factors associated with outcome[12]
Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S)	RCT	CEA / CAS	> 60%	- Stroke or death within 30 days of procedure and at 6 months[13] - stroke or death within 30 days of procedure and at 4 years[14] - Sex-specific 30-day risk of death, any stroke and 4 year risk of ipsilateral stroke (combined) [14] - Stroke or death at 5 years and 10 years[15]
Basel Carotid Artery Stenting Study (BACCAS)	RCT	CEA / CAS	> 70%	- 30-day risk of stroke, death, and myocardial infarction[16] - patency of vessel after 2 years[16]
Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST)	RCT	CEA / CAS	> 50%* > 60%†	- stroke, myocardial infarction, death within 30 days of randomization[17] - ipsilateral stroke at 4 years[17] - Sex-specific 30-day and 4 year risk of myocardial infarction, stroke, or death (composite and individual components)[18] - Myocardial infarction, stroke, death and other adverse events during the periprocedural period[19] - 30-day and/or 10-year risk stroke, myocardial infarction, death (composite outcome)[20]

Study	Study Type	Interventions	Percent Stenosis	Outcome Assessed
				- Sex-specific 30-day and 10 year risk of primary composite outcome[20]
International Carotid Stenting Study (ICSS) Investigators	RCT	CEA / CAS	> 50%	- 120-day risk of stroke, death, or myocardial infarction (composite)[21] - Sex-specific 120-day risk of the composite outcome[21] - 7-year longitudinal collection of stroke, death, or myocardial infarction events[22]
NASCET and ECST	IPD Meta-Analysis	CEA / BMT	0-99%	- Risk of ipsilateral ischemic stroke, determined in relation to time from the last symptomatic event to randomization (sex-specific data available)[23] - 5-year risk of ipsilateral ischemic stroke and any stroke or death within 30 days of randomization [combined][24] - 5-year risk of ipsilateral ischemic stroke and any stroke or death within 30 days of randomization [combined], stratified by percent stenosis[24]
EVA-3S, SPACE, ICSS, CREST trials	IPD Meta-Analysis	CEA / CAS	Multiple	Associations between perioperative and clinical variables and the 30-day risk of stroke or death[25] - Multiple outcomes assessed within 120 days and at 5 years[26] - Sex-specific outcomes of 120-day risk of any stroke or death

Study	Study Type	Interventions	Percent Stenosis	Outcome Assessed
				and 5-year risk of ipsilateral stroke (combined)[26] - Sex-specific outcome of 5 year risk of ipsilateral stroke[26]
EVA-3S, SPACE, BACASS, ICSS, CREST trials	IPD Meta-Analysis	CEA / CAS	Multiple	- Multiple outcomes assessed at 30 days after treatment (stroke, death, ipsilateral stroke, disabling stroke, myocardial infarction, restenosis etc.)[27] - Sex-Specific outcomes for death or any stroke within 30 days of treatment[27]

CEA: Carotid endarterectomy; IPD: individual patient data; RCT: randomized controlled trial
*Denotes Symptomatic Stenosis; †Denotes Asymptomatic Stenosis

Supplemental Table III: Baseline Female Patient Characteristics of the Primary Studies

	ECST (1998)[8]	Rothwell et al.[5]	Alamowitch et al.[9]*	SPACE (2006)[10]	Eckstein et al. (SPACE)[11]	Mas et al. (EVA-3S)[12]	Ederle et al. (CAVATAS)[13]	ICSS[14]	Howard et al. (CREST)[3]	Brott et al.[15]	Brott et al.[16]	Muller et al. (2020)[17]
n	850	1718	1208	334	338	130	152	503	872	872	1437	1466
Age (years)	NR	NR	34.8%†	NR	NR	NR	NR	NR	69.2 (9.2)	NR	NR	NR
Hypertension	NR	NR	66.6%	NR	NR	NR	NR	NR	88.3%	NR	NR	NR
Diabetes	NR	NR	22.7%	NR	NR	NR	NR	NR	31.6%	NR	NR	NR
Dyslipidemia	NR	NR	42.0%	NR	NR	NR	NR	NR	84.4%	NR	NR	NR
Present Smoker	NR	NR	34.3%	NR	NR	NR	NR	NR	27.7%	NR	NR	NR
Previous TIA/Stroke	NR	NR	18.1%	NR	NR	NR	NR	NR	NR	NR	NR	NR
50%-69% Stenosis	NR	NR	24.2%	NR	NR	NR	NR	NR	NR	NR	NR	NR
>70% Stenosis	NR	NR	41.8%	NR	NR	NR	NR	NR	NR	NR	NR	NR

NR: not reported

*Baseline patient characteristics for NASCET and ACE trials reported together

†Reported “Age older than 70 years” in percent

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