Cognitive Outcomes After Cardiovascular Procedures in Older Adults: A Systematic Review

Appendices

November 17, 2014

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. HHSA-290-2007-10064

Prepared by:
Minnesota Evidence-based Practice Center
Minneapolis, MN

Investigators:
Howard A. Fink, M.D., M.P.H.
Laura S. Hemmy, Ph.D.
Roderick MacDonald, M.S.
Maureen H. Carlyle, M.P.H.
Carin M. Olson, M.D., M.S.
Maurice W. Dysken, M.D.
J. Riley McCarten, M. D.
Robert L. Kane, M.D.
Indulis R. Rutks, B.S.
Jeannine Ouellette
Timothy J. Wilt, M.D., M.P.H.

Contents

Appendix A. Study Protocol ……..……...…….....A-1

Appendix B. Excluded Studies …….B-1

Appendix C. Search Strategy ……...C-1

Appendix D. Neuropsychological Test Descriptions ……....……...D-1

Appendix E. Summary of Baseline Characteristics
Table 1. Summary of Baseline Characteristics – All Studies ……E-1
Table 2. Summary of Baseline Characteristics – CABG Studies ……..E-2
Table 3. Summary of Baseline Characteristics – AVR Studies ……E-3
Table 4. Summary of Baseline Characteristics – CAS / CEA Studies ……E-4

Appendix F. Assessment of Individual Study Quality / Risk of Bias
Table 1. Assessment of Individual Study Quality – Randomized Controlled Trials F-1
Table 2. Assessment of Individual Study Quality – Observational Studies F-2

Appendix G. Evidence Tables
Table 1. Evidence table: Coronary Artery Bypass Grafting Studies ……..G-1
Table 2. Evidence table: Aortic Valve Replacement Studies ..…….G-14
Table 3. Evidence table: Carotid Artery Stenting and Endarterectomy ….……..G-17

Appendix H. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment
Table 1. Clinically Diagnosed Cognitive Impairment: CABG ..……H-1
Table 2. Clinically Diagnosed Cognitive Impairment: AVR ……H-4
Table 3. Clinically Diagnosed Cognitive Impairment: CAS and CEA …….……H-5

Appendix I. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests
Table 1. Incident Cognitive Impairment: CABG ……I-1
Table 2. Incident Cognitive Impairment: AVR ……..……I-6
Table 3. Incident Cognitive Impairment: CAS and CEA ……I-7

Appendix J. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains
Table 1. Cognitive Domains: CABG …….…….....J-1
Table 2. Cognitive Domains: AVR …….…….……J-21
Table 3. Cognitive Domains: CAS and CEA ……..……J-27

Appendix K. Stroke/TIA Outcomes Tables
Table 1. Stroke/TIA Outcomes: CABG ……..……K-1
Table 2. Stroke/TIA Outcomes: AVR ……K-2
Table 3. Stroke/TIA Outcomes: CAS and CEA ……K-3

Appendix L. Strength of Evidence Tables
Table 1. Strength of Evidence for CABG studies …….....L-1
Table 2. Strength of Evidence for AVR studies …….L-9
Table 3. Strength of Evidence for CAS / CEA studies ……L-11

Appendix M. Mean Change from Baseline Tables
Table 1. Mean change from baseline for Trail Making A: CABG studies M-1
Table 2. Mean change from baseline for Trail Making A: CAS studies M-2
Table 3. Mean change from baseline for Trail Making A: CEA studies M-2
Table 4. Mean change from baseline for Verbal Fluency: CABG M-3
Table 5. Mean change from baseline for RAVLT: CABG M-3
Table 6. Mean change from baseline for RAVLT: CAS M-5
Table 7. Mean change from baseline for RAVLT: CEA M-5
Table 8. Mean change from baseline for Trail Making B: CABG M-6
Table 9. Mean change from baseline for Trail Making B: CAS M-7
Table 10. Mean change from baseline for Trail Making B: CEA M-7
Table 11. Mean change from baseline for Grooved Pegboard Test: CABG M-8
Table 12. Mean change from baseline for Grooved Pegboard Test: CAS M-10
Table 13. Mean change from baseline for Grooved Pegboard Test: CEA M-10
Table 14. Mean change from baseline for Digit Span Test: CABG M-11
Table 15. Mean change from baseline for Digit Symbol Test: CABG M-13
Table 16. Mean change from baseline for Block Design: CABG M-14
Table 17. Mean change from baseline for Boston Naming Test or Vocabulary WAIS III: CABG M-15
Table 18. Mean change from baseline for Mini Mental State Exam: CABG M-15
Table 19. Mean change from baseline for Montreal Cognitive Assessment: CABG M-16
Table 20. Mean change from baseline for Mini Mental State Exam: CEA M-16
Table 21. Mean change from baseline for Montreal Cognitive Assessment: CEA M-17
Table 22. Mean change from baseline for Mini Mental State Exam: AVR M-17
Table 23. Mean change from baseline for domains from Altinbas 2011: CAS versus CEA M-18

References ……..R-1

Appendix A

Study Protocol

Evidence-based Practice Center Systematic Review Protocol

Project Title: Impact of Neurological Events upon Cognitive Function following Cardiovascular Procedures: a Systematic Review

I. Background and Objectives for the Systematic Review

Among possible adverse outcomes following cardiovascular (CV) procedures in older adults, including heart attacks (MI), blood clots (DVT/PE), infectious complications, strokes, and delerium, there also has long been a concern regarding possible nontransient adverse cognitive outcomes. Although investigators sought to establish a consensus for cognitive assessment methods following coronary artery bypass grafting (CABG),[1] most early reports are now believed to have overestimated the incidence of adverse cognitive outcomes attributable to these procedures.[2] Though results were based on formal neuropsychological testing, i.e. the standardized administration and qualified interpretation of selected cognitive tests, these studies often did not account for pre-procedure cognitive impairments, transient post-procedure impairments, post-procedure impairments attributable to underlying disease, limitations in cognitive test precision, and the practice effects of repeat cognitive testing.

To address the limitations of these older studies, more recent studies have incorporated pre-procedure cognitive assessments, non-procedure control groups, and limitations on the timing of post-procedure cognitive assessments. A recent systematic review limited to studies reporting results for pre- and post-procedure neuropsychological tests that were recommended in a 1995 consensus paper[1] found that psychomotor speed may be impaired compared to baseline very early after CABG (<2 weeks), but is, along with memory and executive functioning, improved compared to baseline by 3 months and remains so 6-12 months after the procedure.[3, 4] This review was limited, however, in that it did not evaluate other neuropsychological domains, longer term neuropsychological test results, or whether neuropsychological test abnormalities were associated with symptoms or functional impairment. This is an important consideration since patients are likely to be more concerned about procedure-related cognitive risks that are not just measurable on neuropsychological testing, but also are associated with symptoms they recognize and even moreso that adversely impact their social, occupational or other daily functioning.

Several patient characteristics have been associated with adverse cognitive outcomes after CABG, including advanced age, fewer years of education, limited social support, cerebrovascular or peripheral vascular disease, hypertension, diabetes, and depression.[2, 5-8] However, we are unaware of any systematic reviews that have examined these associations. With regard to the possible impact of procedure-related factors on post-CABG cognitive outcomes, multiple reviews suggest no increased cognitive risk with on-pump versus off-pump CABG.[3, 9] However, less is known about the impact of other procedure-related factors on cognitive outcomes, including from procedural or peri-procedural stroke or TIA.

In a recent systematic review[10] of 47 studies of carotid revascularization (carotid endarterectomy [CEA] and/or carotid artery stenting [CAS]), about half reported improvement in at least one cognitive measure after the procedure, and about half reported some decline or no change. Authors suggested that the variable findings could be explained by the small sample size of many studies (about one-fourth had fewer than 25 participants with CEA or CAS), variable follow-up times (including about one-fourth with follow-up of <1 month), and different neurocognitive tests administered. In addition, about one-third of included studies did not compare cognitive changes to those in a control group that did not undergo CEA or CAS, another potential source of bias. Clarifying the true association between CEA and CAS and post-procedure cognitive outcomes will require a more selective consideration of available studies, distinguishing between those most and least likely to provide biased results. This will be a first step before the impact of procedure-related factors and patient characteristics on post-CEA and post-CAS cognitive outcomes can be evaluated.

Data on cognitive outcomes after other CV procedures, including open and transcatheter cardiac valve replacement/repair and atrial fibrillation ablation appear more limited. We are unaware of any review addressing the degree to which these procedures cause adverse cognitive outcomes, including their clinical severity, duration, and pattern of neurocognitive domain impairment.

Though recent American College of Surgery/American Geriatrics Society Guidelines recommend pre-operative cognitive screening of all patients aged >65 years, including a history and a formal cognitive assessment, such as with the brief, mini-Cog screening measure,[11] the extent to which this occurs in current practice is unknown. Current uncertainties regarding the course, severity, and pattern of cognitive outcomes attributable to CABG, CEA, CAS, cardiac valve replacement/repair, and atrial fibrillation ablation limit pre-procedure discussions between clinicians and patients regarding what cognitive risks may be associated with these procedures. Enhanced understanding of these issues has the potential to inform these discussions and potentially lead to safer and more targeted use of these procedures. The proposed systematic review will comprehensively characterize the cognitive outcomes associated with these CV procedures, and the extent to which these associations are modified by procedure and patient characteristics.

Our findings should provide information about the characteristics and predictors of any cognitive outcomes associated with these CV procedures. Further, they should define the limitations of existing evidence and the parameters of any future RCTs or other research studies that are needed to address remaining evidence gaps.

II. The Key Questions

1. **In older adults who undergo selected cardiovascular procedures, what are the associated post-procedure cognitive outcomes?** (e.g. clinical severity; timing/duration; pattern of cognitive domain impairment)
2. **In older adults who undergo selected cardiovascular procedures, are associated risks for post-procedure adverse cognitive outcomes affected by procedural and peri-procedural stroke or transient ischemic attack (TIA) and other procedure characteristics?** (e.g. alternative procedures for same indication, such as surgical vs. catheter-based/stenting; anesthesia type; adjunctive neuroprotective treatments)
3. **In older adults who undergo selected cardiovascular procedures, are associated risks for post-procedure adverse cognitive outcomes affected by patient characteristics?** (e.g. age; baseline cognitive function; past stroke or TIA, baseline cardiovascular disease [CVD] severity; hypertension; diabetes; depression)

- **Population(s):**
  - For all 3 key questions:
    1. Older adults undergoing selected CV procedures. There will be no limitations on the basis of cardiac or cerebrovascular disease severity, comorbidities or patient demographics other than age.
    2. We do not anticipate that participant inclusion/exclusion criteria for any eligible studies will exactly match Medicare eligibility. To maximize our report findings to the majority of Medicare enrollees, those aged 65 years or older, as a first step we will include studies that are entirely comprised of individuals aged 65 years or older or that report subgroup data from at least 10 patients in this age stratum. However, we anticipate that these criteria alone would exclude data from many study participants in this older age range who enrolled in studies that also include some younger participants and didn't report stratified data by age. Therefore, we also will include studies that reported that at least half of participants were 65 years or older, or that reported either a mean or median age of 65 years or older. We do not plan to search for studies that enrolled participants with ESRD or Medicare qualifying disabilities.
  - For key question 3 only:

1. To evaluate whether impact of CV procedures on cognitive outcomes differs according to patient characteristics, we will evaluate results for subgroups defined by selected participant characteristics that may increase risk of adverse cognitive outcomes. Identification of patient characteristics associated with adverse post-procedure cognitive outcomes may help predict individual patient risks. Identifying the subset of these predictors that are potentially modifiable may identify targets for future interventions to reduce these risks. Potential patient characteristics to be evaluated may include: age; baseline cognitive function; past stroke or TIA, baseline CVD severity; hypertension; diabetes; and depression.

- **Interventions (Procedures):**
  - We will evaluate each of the 3 key questions separately for each of the following CV procedures:
    1. Coronary artery revascularization (e.g. coronary artery bypass grafting [CABG], percutaneous coronary intervention [PCI])*
    2. Carotid artery revascularization (e.g. carotid endarterectomy [CEA], carotid artery stenting [CAS])*
    3. Cardiac valve replacement/repair (e.g. surgical or transcatheter, aortic or mitral)
    4. Atrial fibrillation ablation (e.g. surgical, catheter)

    *Also including combined coronary and carotid artery revascularizations
  - For key question 2 only:
    1. To evaluate whether impact of CV procedures on cognitive outcomes differs according to procedure characteristics, we will compare whether results differ as a function of whether patients had a procedural or peri-procedural stroke or TIA; between different procedures used for the same clinical indication, such as surgical vs. catheter-based/stenting; and as a function of procedure time, anesthesia time or type, or use of adjunctive neuroprotective treatment..

- **Comparators:**
  - For randomized controlled trials of CV procedures, comparison subjects may include those assigned to placebo, usual care, or active control (e.g. nonprocedure medical management, or an alternative CV procedure, including possible percutaneous procedures).
  - For observational studies, in an effort to limit potential selection bias, we will only include studies that compare the procedure group to an appropriate control group. This control group may be a matched comparison group of patients who did not undergo the specific CV procedure within the past year or another group in which analyses accounted for differences in underlying CVD severity and other factors between patients who did and did not undergo CV procedures (e.g. age, CVD risk factors, other comorbidities, baseline cognitive function, past stroke or TIA).
  - Historical controls will not be considered eligible because of our concern that CVD treatment, including surgical and catheter-based techniques and adjunctive therapy may have changed over time. Even the types of patients who undergo these procedures may have changed over time. All these changes may affect the risk of post-procedure cognitive impairment. Therefore, it would not be possible from studies that use historical controls to accurately assess whether changes in post-procedure cognitive outcomes are due to the procedures or to historical trends in health care and/or populations enrolled. This could result in biased findings.

- **Outcome measures for all questions:**
  - ***Primary outcomes***

Our two primary outcomes both involve new onset, post-procedure symptomatic changes in cognition. In both cases, these adverse cognitive symptoms, such as poor short-term memory or language abilities, may be recognized by the patient, informant, or both. However, because self-report of cognitive symptoms is not always accurate or reliable, at least in part due to the high prevalence of impaired insight among patients with cognitive impairment, we also will require that studies confirmed these symptoms with neuropsychological testing.
Neuropsychologically confirmed cognitive symptoms may or may not be severe enough to be associated with functional impairment (e.g. occupational, social, activities of daily living). Post CV-procedure functional impairments unrelated to cognition (e.g. attributable to impaired CV function, strength, and/or coordination) will be considered out of scope for this review.

1. **Confirmed symptomatic cognitive impairment associated with functional impairment.** Patients with impairment in memory plus at least one other cognitive domain, who have associated functional impairment, meet DSM-IV criteria for dementia.[12] Patients with impaired function, but with a different pattern of neuropsychological impairment (e.g. only one impaired cognitive domain, only nonmemory domain(s) impaired) may be considered for alternative diagnoses (e.g. possible dementia).
2. **Confirmed symptomatic cognitive impairment not associated with functional impairment.** Patients with impairment limited to one or two cognitive domains, who have no associated functional impairment meet Peterson criteria for mild cognitive impairment (MCI). Patients with intact function, but with a different pattern of neuropsychological impairment (e.g. impairment in three or more cognitive domains) may be considered for alternative diagnoses (e.g. cognitive impairment no dementia [CIND], cognitive impairment etiology unknown).

Within these two primary outcome categories, we also will record if studies report specific etiologies and/or apply specific diagnostic labels for cognitive impairment outcomes (e.g. dementia, vascular dementia, cognitive impairment not dementia secondary to cerebrovascular disease, MCI). However, if studies report these etiologies/diagnostic labels without indicating how they were confirmed by neuropsychological testing (e.g. study reported ICD-9 administrative codes only), we will report diagnostic information derived from these studies separately.

- ***Secondary outcomes***
  Our secondary outcome will be **clinically meaningful magnitude of change in neuropsychological test performance**. This will be defined as weighted mean differences (between group differences in change from baseline to follow-up) of at least small effect size in one or more neuropsychological tests, independent of whether these test results were correlated with clinical symptoms or functional impairment. These neuropsychological tests are performance-based and include both brief, global cognitive screening measures (e.g. mini-mental status exam [MMSE], mini-Cog, MOCA) and more narrow measures that evaluate one or more specific cognitive domains (i.e. attention, memory, language, executive, visual-spatial functioning, and psychomotor speed).
- ***Intermediate outcomes***
  Measures of continuous change in neuropsychological test performance are of uncertain clinical importance and will not be considered outcomes for the purpose of this report. Procedural and peri-procedural stroke and TIA also will not be considered outcomes in themselves for the purpose of this report. Instead, they will be considered as possible mediators in the causal pathway between CV procedures and the primary and secondary cognitive outcomes listed above.

- **Timing**:
  - ***Pre-procedure***
    1. All eligible cohort studies must have performed neuropsychological

testing prior to the CV procedure. Randomized controlled trials may be eligible without pre-procedure neuropsychological testing.

- ***Post-procedure***
    1. All eligible studies must have performed cognitive evaluations at least 3 months after the CV procedure in an effort to eliminate transient effects on cognition from factors other than the procedure, including pain, anesthesia, medications, sleep deprivation, and hospital-related illness. In addition, results from testing performed this soon after pre-procedure testing may be influenced by practice effects.
    2. We will extract and separately report cognitive outcomes measured 3 to 12 months after the CV procedure (intermediate-term), and those measured >1 year after the procedure (long-term). For each study, data for a given outcome will only be extracted for the latest available time point within each of these two time periods. We suspect that in most cases changes reported as present between 3 to 12 months post-procedure were present earlier but persisted, sometimes after resolution of superimposed, transient, nonprocedure-related factors. We will evaluate cognitive outcomes reported >1 year after the CV procedure to look at duration of cognitive changes that were reported 3 to 12 months after the procedure, progression of these earlier changes, and to identify cognitive outcomes that first became evident >1 year after the procedure. Use of RCTs or observational studies with well-matched control groups will be essential for distinguishing the extent to which cognitive changes first reported >1 year after the procedure and progression of earlier cognitive changes were caused by the CV procedure and the extent to which they were attributable to progression of an unrelated underlying disease.

- **Settings:**
    - Studies will be eligible regardless of whether the CV procedure took place in the inpatient or outpatient setting. However, because of the high rate of delirium reported in older hospitalized patients,[13] studies in which post-procedure cognitive assessments are available only from within the inpatient setting will be excluded. This restriction is intended to limit the impact of factors other than the CV procedure on reported cognitive outcomes (e.g. pain, anesthesia, medications, sleep deprivation, and hospital-related illness unrelated to the procedure). Studies may be limited to those conducted in Western settings (or stratified on this factor) to increase the applicability of findings to U.S. practices and outcomes.

III. Analytic Framework

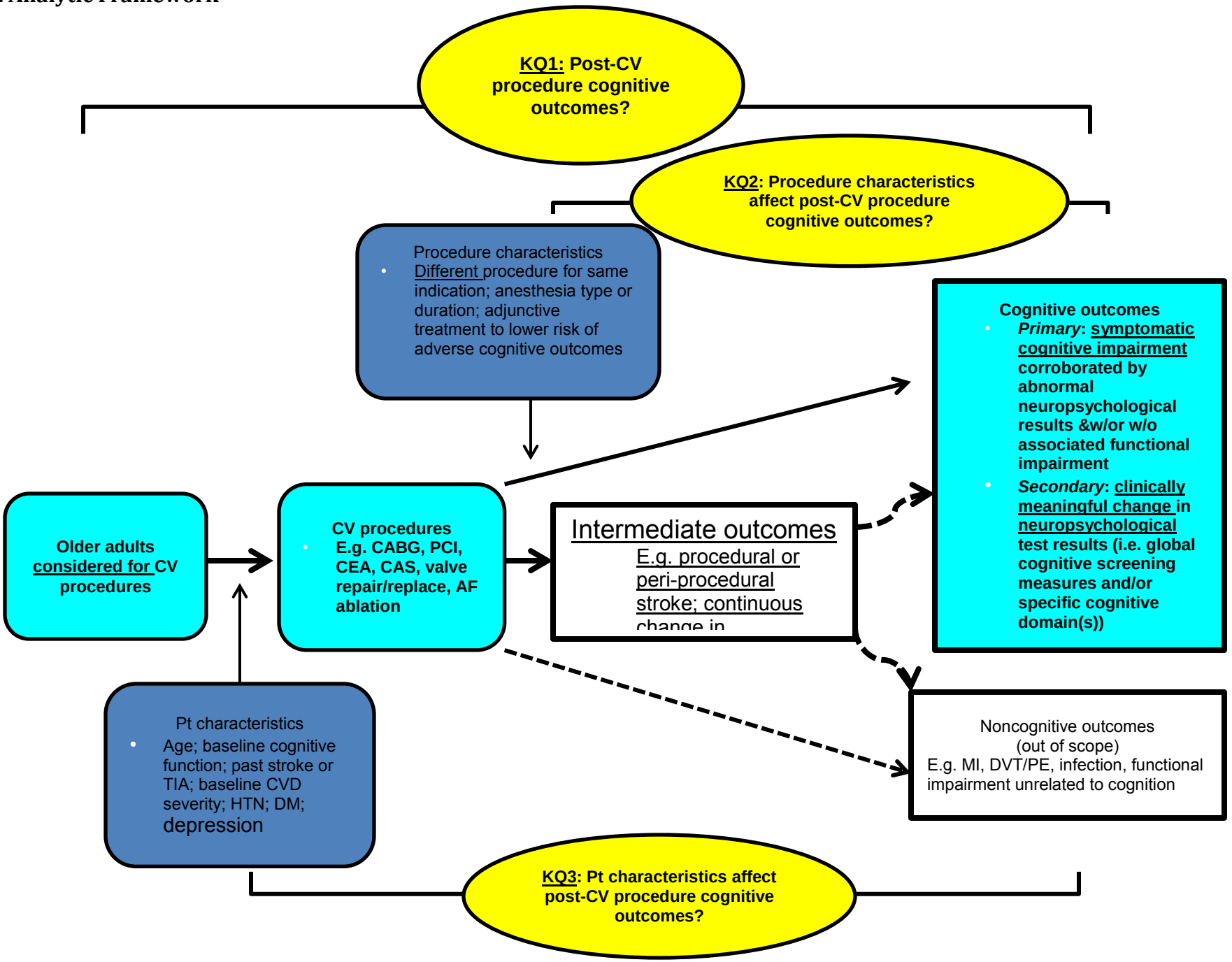

Figure 1.

AF = atrial fibrillation; CABG = coronary artery bypass grafting; CAS = carotid artery stenting; CEA = carotid endarterectomy; CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; DVT = deep venous thrombosis; HTN = hypertension; PCI = percutaneous coronary intervention; PE = pulmonary embolism; TIA = transient ischemic attack

IV. Methods

A. Criteria for Inclusion of Studies in the Review

- Study design: Randomized controlled trial (RCT), nonrandomized comparative trial, prospective observational cohort study, or systematic review that reports separable results for these study types only.
- Population:
    1. Participants must have been older adults. As discussed above, we will include studies whose participants are all aged ≥65 years, have a mean or median age ≥65 years, or that report subgroup data from ≥10 patients aged ≥65 years.
    2. Participants in at least one intervention or observation arm underwent one of the CV procedures of interest
        a. Coronary artery revascularization (e.g. coronary artery bypass grafting [CABG], percutaneous coronary intervention [PCI])*
        b. Carotid artery revascularization (e.g. carotid endarterectomy [CEA], carotid artery stenting [CAS])*
        c. Cardiac valve replacement/repair (e.g. surgical or transcatheter, aortic or mitral)
        d. Atrial fibrillation ablation (e.g. surgical, catheter)

        *Also including combined coronary and carotid artery revascularizations
- Minimum sample size of ≥10 participants in each treatment arm for RCTs and ≥50 participants in each arm for nonrandomized comparative studies and prospective cohort studies.
- Publication date range: To limit the review to evaluating cognitive outcomes after CV procedures that reasonably reflect current clinical practice, all studies must have been published since 1990.
- As stated earlier, nonrandomized comparative studies and prospective cohort studies must have performed pre-procedure neuropsychological assessments, including possibly brief global cognitive screening measures. RCTs may be included whether or not they performed pre-procedure neuropsychological assessments.
- As stated earlier, all eligible studies must have reported at least one primary or secondary cognitive outcome at least 3 months after the procedure that was measured outside of the acute inpatient setting.
- As stated earlier, all studies must have included a nonhistorical control group that did not undergo the CV procedure of interest or that underwent a modified version of the procedure
- All studies must have been published in English language

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions We will identify evidence for this review by searching relevant bibliographic databases. Bibliographic database searching will utilize MEDLINE, the Cochrane Central register of controlled trials (CENTRAL), and Scopus to identify RCTs published 1990 to the present. See **Figure 2** for full MEDLINE search strategy. An MLIS research librarian experienced in systematic review search methodology and not involved in the project has peer reviewed and helped refine our bibliographic literature search strategy. Bibliographic database searches will be supplemented with hand searching of reference lists of included studies, and previous systematic reviews. The literature search will be updated while the draft report is under public/peer review.

Additionally, we will search ClinicalTrials.gov to identify relevant registered and completed trials. These sources will be used to identify trials not previously identified. Published and registered trials will be compared to assess potential outcomes reporting bias. Trials registered but not published will be evaluated qualitatively to comment on the potential publication bias relevant to this topic.

Screening of studies identified in our initial and updated literature searches, and of any studies identified during public and peer review will occur in two stages. First, search results will be preliminarily triaged. Titles and abstracts will be reviewed by two independent investigators and marked 'include,' 'exclude,' or 'full text needed' if a determination cannot be made based upon available information. Differences in triage decisions between the two investigators will be resolved by consensus discussion, involving the lead investigator as necessary. Full text will be obtained for articles identified as potential includes during initial triage. These studies will be distributed among investigators for secondary screening and data extraction. Full text will be evaluated by two investigators to ensure that the study meets inclusion criteria. We will document the inclusion and exclusion status and reason for exclusion in the project library of citations.

Figure 2. Draft MEDLINE Literature Search Strategy

Database: Ovid MEDLINE(R) <1946 to January Week 3 2013>
Search Strategy:
---
1 comprehension/ (6633)
2 cognition disorders/ (44130)
3 auditory perceptual disorders/ (909)
4 memory/ (49313)
5 memory, episodic/ (472)
6 memory, long-term/ (371)
7 memory, short-term/ (13113)
8 mental recall/ (25327)
9 retention, psychology/ (7518)
10 memory disorders/ (13433)
11 exp Neuropsychological Tests/ (61191)
12 exp Executive Function/ (3065)
13 exp Psychometrics/ (49676)
14 exp Psychomotor Disorders/ (10067)
15 exp Psychomotor Performance/ (78939)
16 Dementia/ or Alzheimer disease/ or aphasia, primary progressive/ or dementia, vascular/ or frontotemporal lobar degeneration/ or lewy body disease/ (90697)
17 pick disease of the brain/ (351)
18 mild cognitive impairment/ (762)
19 central nervous system dysfunction.mp. (498)
20 neuropsychological impairment.mp. (860)
21 (Cognitive decline or cognitive dysfunction or cognitive tests or cognitive assessment or cognitive function or cognitive evaluation or cognitive performance or cognitive change or cognitive problem or cognitive outcome or cognitive sequelae).mp. (33149)
22 (Neuropsychologic* decline or neuropsychologic* dysfunction or neuropsychologic* tests or neuropsychologic* assessment or neuropsychologic* function or neuropsychologic* evaluation or neuropsychologic* performance or neuropsychologic* change or neuropsychologic* problem or neuropsychologic* outcome or neuropsychologic* sequelae).mp. (62490)
23 or/1-22 (364408)

24 Randomized controlled trials as topic/ (82496)
25 Randomized controlled trial/ (337448)
26 Random allocation/ (75972)

27 Double blind method/ (117175)
28 Single blind method/ (16885)
29 Clinical trial/ (472549)
30 Clinical trial, phase i.pt. (12507)
31 Clinical trial, phase ii.pt. (20105)
32 Clinical trial, phase iii.pt. (7375)
33 Clinical trial, phase iv.pt. (759)
34 Controlled clinical trial.pt. (84963)
35 Randomized controlled trial.pt. (337448)
36 Multicenter study.pt. (149119)
37 Clinical trial.pt. (472549)
38 exp clinical trials as topic/ (259816)
39 (clinical adj trial$).tw. (174974)
40 ((singl$ or doubl$ or treb$ or trip$) adj (blind$3 or mask$3)).tw. (114747)
41 Randomly allocated.tw. (14024)
42 (allocated adj2 random$).tw. (16356)
43 or/24-42 (1021274)

44 Epidemiologic studies/ (5512)
45 exp cohort studies/ (1215732)
46 (cohort adj (study or studies)).tw. (64056)
47 Cohort analy$.tw. (2848)
48 (follow up adj (study or studies)).tw. (33441)
49 (Observational adj (study or studies)).tw. (32538)
50 Longitudinal.tw. (112860)
51 or/44-50 (1316456)

52 Meta analysis/ (36638)
53 Meta analys$.tw. (41461)
54 literature review.mp. (35019)
55 (systematic adj (review or overview)).tw. (30248)
56 or/52-55 (106130)

57 43 or 51 or 56 (2182597)

58 Case report.tw. (170277)
59 letter/ (758034)
60 historical article/ (288506)
61 addresses/ (4019)
62 autobiography/ (2675)
63 Bibliography/ (14862)
64 Biography/ (156977)
65 Comment/ (484716)
66 Editorial/ (307072)
67 News/ (142112)
68 or/58-67 (1755076)

69 57 not 68 (2085235)

70 limit 69 to humans (1980119)
71 limit 70 to yr="1990 -Current" (1694926)
72 limit 71 to english language (1521263)
73 limit 72 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") (423582)
74 72 not 73 (1097681)

75 exp Myocardial Revascularization/ (75825)
76 exp percutaneous coronary intervention/ (32327)
77 Heart bypass, right/ (576)
78 Coronary revascularization.mp. (4172)
79 (coronary artery bypass graft or CABG).mp. (14519)
80 (percutaneous coronary intervention or PCI).mp. (15273)
81 coronary stent*.mp. (4595)
82 coronary angioplas*.mp. (11666)
83 or/75-82 (89913)

84 74 and 83 (28370)

85 exp Endarterectomy, Carotid/ (6306)
86 (carotid endarterectomy or CEA).mp. (20384)
87 (carotid artery stenting or CAS).mp. (54374)
88 carotid surg*.mp. (1111)
89 or/85-88 (76271)

90 74 and 89 (6030)

91 Heart valve prosthesis/ (26828)
92 exp Heart Valve Prosthesis Implantation/ (11217)
93 Cardiac valve annuloplasty/ (137)
94 (aortic valve replacement or AVR).mp. (8953)
95 (mitral valve replacement or MVR).mp. (5610)
96 (aortic valve repair or mitral valve repair).mp. (2378)
97 (aortic valve surg* or mitral valve surg*).mp. (2156)
98 or/91-97 (41284)

99 74 and 98 (5753)

100 exp Catheter Ablation/ (18600)
101 exp Ablation Techniques/ (82421)
102 100 or 101 (82421)

103 exp Atrial Fibrillation/ (30442)
104 atrial fibrillation ablation.mp. (446)
105 103 or 104 (30482)

106 102 and 105 (5004)

107 74 and 106 (1659)

108 23 and 84 (396)

109 23 and 90 (112)

110 23 and 99 (40)

111 23 and 107 (4)

112 or/108-111 (527)

C. Data Abstraction and Data Management

Two investigators will act as primary and secondary abstractor/evaluators, respectively, for their assigned studies. Data fields to be extracted will be determined for each key question/subquestion. Data elements likely will include author; year of publication; CV procedure intervention and control regimens; anesthesia type and duration; description of adjunctive treatments intended to lower risk of adverse cognitive outcomes; sample size; subject inclusion and exclusion criteria; participant baseline age, prevalence of hypertension, diabetes, stroke/cerebrovascular disease, and depression; type(s) of pre-procedure neuropsychological assessment (e.g. specific brief global cognitive screening measures and specific cognitive domains tested); N, mean and SD for each reported pre-procedure neuropsychological test; incidence of procedural and peri-procedural stroke and/or TIA; timing and definition of clinical post-procedure cognitive outcomes; event rates for clinical post-procedure cognitive outcomes (n/N reporting these outcomes, clearly designating drop-outs); and timing, type, n/N reporting, mean and SD for each post-procedure neuropsychological test.

Authors of studies otherwise meeting eligibility criteria, but not reporting mean and SD for pre- and post-procedure neuropsychological testing will be contacted seeking this additional information. When these results are not directly reported by the study, but can be calculated from available data, we will perform these calculations. The primary abstractor/evaluator will extract relevant data from studies meeting inclusion criteria onto pre-tested extraction forms/evidence tables. These extraction forms/evidence tables will be reviewed and verified for accuracy by the secondary abstractor/evaluator. Differences in abstraction between the two investigators will be resolved by consensus discussion, involving the lead investigator as necessary. As discussed above, timing of post-procedure cognitive assessments will be categorized into those measured at 3 to 12 months (intermediate-term) and those measured >1 year after the procedure (long-term). For each study, we will record all timepoints at which post-procedure cognitive assessments were performed, but will report results for only the latest assessment of each cognitive outcome within each of these two time period.

D. Assessment of Methodological Risk of Bias of Individual Studies

We will evaluate the risk of bias in individual studies according to recommendations from the Cochrane Handbook for Systematic Reviews of Interventions.[14] Following categorization of studies according to their design as either interventional (RCTs, nonrandomized controlled clinical trials) or prospective observational cohort studies, a primary and secondary abstractor/evaluator will independently review study risk of bias for up to two outcomes per study, with one collective rating for clinical outcomes (for confirmed symptomatic cognitive impairment with and without associated functional impairment considered together) and one collective rating for neuropsychological test outcomes.

For interventional studies, we will evaluate risk of bias using criteria from the Cochrane Risk of Bias tool:[15] (1) random allocation of the subjects to the treatment groups; (2) adequacy of allocation concealment, based on the approach by Schulz and Grimes;[16] (3) masking of the outcome assessment (participant, investigator, and/or outcome assessor); (4) use of intention-to-treat principles (i.e. inclusion of all randomized participants in outcomes analyses); and (5) selective reporting of prespecified outcomes. Generally, we will assume a low risk of bias when individual interventional studies meet all quality criteria, a moderate risk of bias if at least one of the quality criteria is not met, and a high risk of bias if multiple quality criteria are not met.[17] We will conclude an unknown risk of bias for the interventional studies with poorly reported quality criteria.

For prospective observational cohort studies, we will assess risk of bias using criteria suggested in the AHRQ Methods Guide:[17] (1) selection bias (use of appropriately comparable control group, design/analysis accounted for important confounding and modifying variables); (2) masking of the outcome assessment (outcome assessor); (3) use of intention-to-treat principles (i.e. inclusion of all comparison group participants in outcomes analyses); (4) attrition bias (if overall or differential dropout/loss to follow-up or exclusions a concern,

missing data appropriately handled); and (5) selective reporting of prespecified outcomes. Generally, we will assume a low risk of bias when individual prospective observational cohort studies meet all quality criteria, a moderate risk of bias if at least one of the quality criteria is not met, and a high risk of bias if multiple quality criteria are not met.[17] We will conclude an unknown risk of bias for the prospective observational studies with poorly reported quality criteria.

Differences in risk of bias assessments between the two investigators will be resolved by consensus discussion, involving the lead investigator as necessary.

E. Data Synthesis

When the patient populations, CV procedures, study designs, and outcomes are clinically comparable, we will perform a quantitative meta-analysis of results for confirmed symptomatic cognitive impairment with associated functional impairment, confirmed symptomatic cognitive impairment without associated functional impairment, and possibly for the outcomes of dementia, MCI, vascular dementia, and for cognitive impairment not dementia secondary to cerebrovascular disease. Under similar conditions, we also will perform a quantitative meta-analysis of results for each brief global cognitive screening test and for up to one neuropsychological test within each cognitive domain. We will analyze data using Review Manager (RevMan) version 5.1 software.[18] We will use random effects models to generate pooled estimates of relative risks and 95% confidence intervals for the incidence of the primary outcomes, and weighted mean differences (between group differences in change from baseline to follow-up) and corresponding effect sizes and 95% confidence intervals for the neuropsychological test outcomes. We will summarize statistical heterogeneity by using the I^2 statistic (50 percent indicates moderate heterogeneity and 75 percent or greater indicates high heterogeneity).[14]

To investigate the possible effect of procedure-related factors on the association between CV procedures and adverse cognitive outcomes, we will consider the following subgroup analyses: incidence of procedural or peri-procedural stroke or TIA; different procedures for the same clinical indication, such as surgical vs. catheter-based/stenting; anesthesia type and duration; procedure duration; and use of adjunctive neuroprotective treatments.

To investigate the possible effect of patient characteristics on the association between CV procedures and adverse cognitive outcomes, we will consider the following subgroup analyses: age; baseline cognitive function; past stroke or TIA, baseline cardiovascular disease [CVD] severity; hypertension; diabetes; and depression.

We will consider random-effects inverse weighted meta-regression on drop-out rate, and, when subgroup analyses are not possible, on the patient characteristics listed above.

Within each CV procedure category, results will first be organized by study design (RCT, nonrandomized comparative studies, prospective observational cohort). Within each type of study design, results will be organized by cognitive outcome, with the primary outcomes reported first, followed by the neuropsychological test results organized by brief global cognitive screening tests and specific cognitive domains (attention, memory, language, executive, visual-spatial functioning, psychomotor speed). Results for each cognitive outcome then will be organized into intermediate- (3 to 12 months) and long-term (>1 year) post-procedure assessments and summarized qualitatively.

Next, results for the primary outcomes will be summarized using weighted risk differences and 95% confidence intervals. These results will be derived by comparing the group-specific incidence of participants reaching these endpoints from among all those in each comparison group. Results for clinical diagnoses not supported by documented neuropsychological test results will not be pooled with studies reporting these outcomes supported by neuropsychological test results or with each other.

Results for the different neuropsychological test results will be summarized by type using weighted mean differences and corresponding standard effect sizes and 95% confidence intervals. These results will be derived by comparing the difference between the intervention and comparison groups in pre- versus post-procedure mean (+/-SD) scores.

Risk of bias ratings may be utilized to conduct sensitivity analysis of results, such as by including and excluding studies with an overall poor rating to assess the influence of poor studies on results of the systematic review.

F. Grading the Strength of Evidence (SOE) for Individual Outcomes The overall SOE for the studies included in this review will be evaluated using methods developed by the Agency for Healthcare Research and Quality (AHRQ) and the Effective Health Care Program[19] and currently being updated.

Within each CV procedure comparison examined, we will evaluate SOE separately for RCTs, nonrandomized comparative studies, and prospective observational cohort studies. For each of these study types with eligible data, SOE will be evaluated separately for the following clinical outcomes: confirmed symptomatic cognitive impairment with associated functional impairment, confirmed symptomatic cognitive impairment without associated functional impairment, and for each brief global cognitive screening test and each of the following cognitive domains (attention, memory, language, executive, visual-spatial functioning, and psychomotor speed). We then will consider the results from the different study designs together and report a single SOE for each of these cognitive outcomes for each examined CV procedure. SOE ratings will be performed independently by two senior reviewers, with differences between the two investigators resolved by consensus discussion, involving the lead investigator as necessary.

In each case, strength of the evidence will be evaluated based on the following domains: (1) study limitations (risk of bias or internal validity); (2) directness; (3) consistency; (4) precision; and, when appropriate, (5) reporting bias. Study limitations will be rated as low, medium or high based on the study design and risk of bias of individual studies. Directness will be rated as direct or indirect based on whether evidence provides a single, direct link between intervention and outcomes. Consistency will be rated as consistent, inconsistent, or unknown (e.g. single study) based on the degree to which included studies appear to have the same direction or magnitude of effect. Precision will be rated as precise, imprecise, or unknown based on the degree of uncertainty surrounding the effect estimate that is attributable to insufficient sample size and/or the number of outcome events. An imprecise estimate would be one in which the effect estimate is wide enough to include clinically distinct conclusions. We will consider rating reporting bias only for RCT evidence and only when the potential SOE for a comparison otherwise is moderate or high. Reporting bias will be rated as suspected or undetected based on detection of publication, outcome and selective analysis reporting bias. Other factors that may be considered in assessing SOE include dose-response relationship, the presence of confounders, and strength of association.

Based on these factors, the overall evidence will be rated qualitatively as:

i. **High**: We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable.
ii. **Moderate**: We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
iii. **Low**: We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.

iv. **Insufficient**: We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding judgment.

An overall rating of high strength of evidence would imply that the included studies were RCTs with a low risk of bias, with consistent, direct, and precise domains.

G. Assessing Applicability While some conditions that affect applicability of studies to clinical practice are used as exclusion criteria in study selection (i.e., cognitive assessment not done long enough after the CV procedure), others may only be identified through detailed review of the studies. Specific study characteristics that may affect applicability will be noted on evidence tables by study abstractors/evaluators. These characteristics may include, but are not limited to, non-U.S. settings, narrow eligibility criteria, participant age or other comorbid characteristics, and cognitive assessments not typically used in current practice.[20]

V. References

1. Murkin JM, Newman SP, Stump DA, et al. Statement of consensus on assessment of neurobehavioral outcomes after cardiac surgery. Ann Thorac Surg. 1995 May;59(5):1289-95. PMID 7733754.
2. Selnes OA, Gottesman RF, Grega MA, et al. Cognitive and neurologic outcomes after coronary-artery bypass surgery. N Engl J Med. 2012 Jan 19;366(3):250-7. PMID 22256807.
3. Cormack F, Shipolini A, Awad WI, et al. A meta-analysis of cognitive outcome following coronary artery bypass graft surgery. Neurosci Biobehav Rev. 2012 Oct;36(9):2118-29. PMID 22732162.
4. Rudolph JL, Schreiber KA, Culley DJ, et al. Measurement of post-operative cognitive dysfunction after cardiac surgery: a systematic review. Acta Anaesthesiol Scand. 2010 Jul;54(6):663-77. PMID 20397979.
5. Lombard FW, Mathew JP. Neurocognitive dysfunction following cardiac surgery. Semin Cardiothorac Vasc Anesth. 2010 Jun;14(2):102-10. PMID 20478950.
6. Dieleman J, Sauer AM, Klijn C, et al. Presence of coronary collaterals is associated with a decreased incidence of cognitive decline after coronary artery bypass surgery. Eur J Cardiothorac Surg. 2009 Jan;35(1):48-53. PMID 19027312.
7. Ho PM, Arciniegas DB, Grigsby J, et al. Predictors of cognitive decline following coronary artery bypass graft surgery. Ann Thorac Surg. 2004 Feb;77(2):597-603; discussion PMID 14759444.
8. Kadoi Y, Kawauchi C, Ide M, et al. Preoperative depression is a risk factor for postoperative short-term and long-term cognitive dysfunction in patients with diabetes mellitus. J Anesth. 2011 Feb;25(1):10-7. PMID 21161290.
9. Alston RP. Brain damage and cardiopulmonary bypass: is there really any association? Perfusion. 2011 Sep;26 Suppl 1:20-6. PMID 21933818.
10. Goldberg JB, Goodney PP, Kumbhani SR, et al. Brain injury after carotid revascularization: outcomes, mechanisms, and opportunities for improvement. Ann Vasc Surg. 2011 Feb;25(2):270-86. PMID 20926244.
11. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. J Am Coll Surg. 2012 Oct;215(4):453-66. PMID 22917646.
12. Association AP. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, D.C.; 2000.
13. Inouye SK. Delirium in older persons. N Engl J Med. 2006 Mar 16;354(11):1157-65. PMID 16540616.
14. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0. In: Collaboration TC, editor. 5.1.0 ed; 2011.
15. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928. PMID 22008217.
16. Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. Lancet. 2002 Feb 16;359(9306):614-8. PMID 11867132.
17. Viswanathan M, Ansari MT, Berkman ND, et al. Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. 2008PMID 22479713.
18. RevMan RMcpV. Copenhagen:The Nordic Cochrance Centre of the Cochrane Collaboration. 2008.

19. Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions--agency for healthcare research and quality and the effective health-care program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID 19595577.
20. Agency for Healthcare Research and Quality. Assessing the Quality and Applicability of Included Studies. In: Agency for Healthcare Research and Quality, ed Methods Reference Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality,; 2007.

VI. Definition of Terms

AVR	aortic valve replacement
CABG	coronary artery bypass grafting
CAS	coronary artery stenting
CEA	carotid endarterectomy
CV	cardiovascular
CVD	cardiovascular disease
FDA	U.S. Food & Drug Administration
MCI	mild cognitive impairment
MVR	mitral valve replacement
PCI	percutaneous coronary intervention
PFO	patent foramen ovale
RCT	randomized controlled trial
RFTO	request for task order
SOE	strength of evidence
TAVR	transcatheter aortic valve replacement
TIA	transient ischemic attack

VII. Summary of Protocol Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

VIII. Review of Key Questions

Key questions were reviewed and refined as needed by the EPC with input from AHRQ staff and the topic nominator to assure that the questions were specific and explicit about what information is being reviewed. This project will not involve Key Informants or a Technical Expert Panel (TEP), and the key questions will not be posted for public comment.

IX. Key Informants

This project will not involve Key Informants.

X. Technical Experts

This project will not involve a Technical Expert Panel.

XI. Peer Reviewers

Peer reviewers will be invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual peer reviewers. The dispositions of the peer review comments will be documented and will be published three months after the publication of the Evidence report.

Individuals under consideration to serve as peer reviewers will be required to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Individuals will not be eligible to serve as a peer reviewer if they have any financial conflict of interest greater than $10,000. However, individuals who disclose potential business or professional conflicts of interest still may submit comments on draft reports through the separate public comment mechanism.

XII. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest which cumulatively total greater than $1,000 will usually disqualify EPC core team investigators.

XIII. Role of the Funder

This project was funded under Contract No. 290-2007-10064 EPCIII from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer will review contract deliverables for adherence to contract requirements and quality. The authors of this report will be responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Appendix B

Excluded Studies

1. Bypass without missing a beat. The Johns Hopkins medical letter health after 50, 2003. 14(11): p. 1-2, 7. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
2. Abildstrom, H., et al., Cerebral blood flow and cognitive dysfunction after coronary surgery. Annals of Thoracic Surgery, 2002. 73(4): p. 1174-1178. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
3. Abu-Omar, Y. and D.P. Taggart, Off-pump coronary artery bypass grafting. Lancet, 2002. 360(9329): p. 327-329. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
4. Aharon-Peretz, J., et al., Cognitive performance following endarterectomy in asymptomatic severe carotid stenosis. European Journal of Neurology, 2003. 10(5): p. 525-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
5. Ahlgren, E., et al., Neurocognitive impairment and driving performance after coronary artery bypass surgery. European Journal of Cardio-Thoracic Surgery, 2003. 23(3): p. 334-40. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
6. Aldea, G.S., et al. Effect of anticoagulation protocol on outcome in patients undergoing CABG with heparin-bonded cardiopulmonary bypass circuits. The Annals of thoracic surgery, 1998. 65, 425-33. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
7. Aleksic, M., et al., Cognitive function remains unchanged after endarterectomy of unilateral internal carotid artery stenosis under local anaesthesia. European Journal of Vascular & Endovascular Surgery, 2006. 31(6): p. 616-21. POPULATION MEAN AGE <65
8. Al-Ruzzeh, S., et al., Effect of off-pump coronary artery bypass surgery on clinical, angiographic, neurocognitive, and quality of life outcomes: randomised controlled trial. BMJ, 2006. 332(7554): p. 1365. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
9. Altinbas, A. Silent cerebral infarcts after carotid endarterectomy or stenting and the risk of cognitive decline. Stroke Trials Registry, Internet Stroke Center: www.strokecenter.org/trials/, 2006. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
10. Altinbas, A., et al. Silent cerebral infarcts after carotid endarterectomy or stenting and the risk of cognitive decline. A randomized comparison. 17th European Stroke Conference, 2008. DUPLICATE / NOT UNIQUE STUDY
11. Altinbas, A., et al. Silent cerebral infarcts after carotid endarterectomy or stenting and the risk of cognitive decline. A randomized comparison. International Stroke Conference 2009, 2009. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
12. Altobelli Iii, A., et al., Surgical coronary revascularization in the elderly. American Journal of Geriatric Cardiology, 2002. 11(3): p. 157-159. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
13. Andrew, M.J., et al., Mood state as a predictor of neuropsychological deficits following cardiac surgery. Journal of Psychosomatic Research, 2000. 48(6): p. 537-546. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
14. Anon Effect of remote ischemic preconditioning on cognitive function after off-pump coronary artery bypass graft. ClinicalTrials.gov [www.clinicaltrials.gov], 2009. FULL TEXT UNAVAILABLE
15. Antonelli Incalzi, R., et al., Neuropsychologic effects of carotid endarterectomy. Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society, 1997. 19(6): p. 785-94. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
16. Arrowsmith, J.E., et al., Central nervous system complications of cardiac surgery. British Journal of Anaesthesia, 2000. 84(3): p. 378-393. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
17. Attigah, N., et al., Assessment of patients' satisfaction in carotid surgery under local anaesthesia by psychometrical testing--a prospective cohort study. European Journal of Vascular & Endovascular Surgery, 2011. 41(1): p. 76-82. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
18. Baba, T., et al., Early neuropsychological dysfunction in elderly high-risk patients after on-pump and off-pump coronary bypass surgery. Journal of Anesthesia, 2007. 21(4): p. 452-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
19. Baikoussis, N.G., et al., Baseline cerebral oximetry values in cardiac and vascular surgery patients: a prospective observational study. Journal Of Cardiothoracic Surgery, 2010. 5: p. 41. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
20. Baker, R.A., et al., The Octopus II stabilizing system: biochemical and neuropsychological outcomes in coronary artery bypass surgery. Heart Surgery Forum, 2001. 4 Suppl 1: p. S19-23. POPULATION MEAN AGE <65
21. Baker, R.A., et al., Preoperative depression and mortality in coronary artery bypass surgery: preliminary findings. ANZ Journal of Surgery, 2001. 71(3): p. 139-42. NO POST-PROCEDURE MEASURE OF COGNITION
22. Bappu, N.J., et al., Troponin-I release after cardiac surgery with different surgical techniques and post-operative neurological outcomes. McGill Journal of Medicine, 2006. 9(2): p. 88-94. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE

23. Barber, P.A., et al., Cerebral ischemic lesions on diffusion-weighted imaging are associated with neurocognitive decline after cardiac surgery. Stroke, 2008. 39(5): p. 1427-1433. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
24. Barnason, S., et al., Influence of a symptom management telehealth intervention on older adults' early recovery outcomes after coronary artery bypass surgery. Heart & Lung, 2009. 38(5): p. 364-76. NO POST-PROCEDURE MEASURE OF COGNITION
25. Barnes, D.E., et al., Predicting risk of dementia in older adults: The late-life dementia risk index. Neurology, 2009. 73(3): p. 173-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
26. Bar-Yosef, S., et al., Aortic atheroma burden and cognitive dysfunction after coronary artery bypass graft surgery. Annals of Thoracic Surgery, 2004. 78(5): p. 1556-62. NO POST-PROCEDURE MEASURE OF COGNITION
27. Bar-Yosef, S., et al., Prevention of cerebral hyperthermia during cardiac surgery by limiting on-bypass rewarming combination with post-bypass body surface warming: A feasibility study. Anesth Analg, 2004. 99(3): p. 641-646. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
28. Bashein, G., et al., A randomized study of carbon dioxide management during hypothermic cardiopulmonary bypass. Anesthesiology, 1990. 72(1): p. 7-15. POPULATION MEAN AGE <65
29. Basile, A.M., et al., S-100 protein and neuron-specific enolase as markers of subclinical cerebral damage after cardiac surgery: preliminary observation of a 6-month follow-up study. European Neurology, 2001. 45(3): p. 151-9. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
30. Baufreton, C., et al., Brain injury and neuropsychological outcome after coronary artery surgery are affected by complement activation. Annals of Thoracic Surgery, 2005. 79(5): p. 1597-605. POPULATION MEAN AGE <65
31. Baumgartner, W.A., Neurocognitive changes after coronary bypass surgery. Circulation, 2007. 116(17): p. 1879-1881. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
32. Beaty, C.A., et al., The role of head computed tomography imaging in the evaluation of postoperative neurologic deficits in cardiac surgery patients. Annals of Thoracic Surgery. 95(2): p. 548-554. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
33. Bejjani, G., et al., No evidence of memory processing during propofol-remifentanil target-controlled infusion anesthesia with bispectral index monitoring in cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia, 2009. 23(2): p. 175-81. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
34. Berger, K., et al., The association between silent stroke and functional status in an elderly, general population - The MEMO-Study, in Research and Practice in Alzheimer's Disease2005. p. 142-146. FULL TEXT UNAVAILABLE
35. Bergh, C., et al., In the eye of both patient and spouse: memory is poor 1 to 2 years after coronary bypass and angioplasty. Annals of Thoracic Surgery, 2002. 74(3): p. 689-93; discussion 694. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
36. Bhudia, S.K., et al., Magnesium as a neuroprotectant in cardiac surgery: a randomized clinical trial.[Erratum appears in J Thorac Cardiovasc Surg. 2007 Aug;134(2):25A]. Journal of Thoracic & Cardiovascular Surgery, 2006. 131(4): p. 853-61. POPULATION MEAN AGE <65
37. Bo, M., et al., Risk of cognitive decline in older patients after carotid endarterectomy: an observational study. Journal of the American Geriatrics Society, 2006. 54(6): p. 932-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
38. Bokeriia, L.A., et al., Asymmetric cerebral embolic load and postoperative cognitive dysfunction in cardiac surgery. Cerebrovascular Diseases, 2007. 23(1): p. 50-56. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
39. Bokesch, P.M., et al., NMDA receptor antibodies predict adverse neurological outcome after cardiac surgery in high-risk patients. Stroke, 2006. 37(6): p. 1432-1436. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
40. Boodhwani, M., et al., Predictors of early neurocognitive deficits in low-risk patients undergoing on-pump coronary artery bypass surgery. Circulation, 2006. 114(1 Suppl): p. I461-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
41. Borger, M.A., et al., Neuropsychologic impairment after coronary bypass surgery: effect of gaseous microemboli during perfusionist interventions. Journal of Thoracic & Cardiovascular Surgery, 2001. 121(4): p. 743-9. POPULATION MEAN AGE <65
42. Borger, M.A. and V. Rao, Temperature management during cardiopulmonary bypass: Effect of rewarming rate on cognitive dysfunction. Seminars in Cardiothoracic and Vascular Anesthesia, 2002. 6(1): p. 17-20. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
43. Borroni, B., et al., Is mild vascular cognitive impairment reversible? Evidence from a study on the effect of carotid endarterectomy. Neurological Research, 2004. 26(5): p. 594-7. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST

44. Bossema, E., et al., Testing the laterality hypothesis after left or right carotid endarterectomy: no ipsilateral effects on neuropsychological functioning. Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society, 2007. 29(5): p. 505-13. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
45. Bossema, E.R., et al., Does carotid endarterectomy improve cognitive functioning? Journal of Vascular Surgery, 2005. 41(5): p. 775-81; discussion 781. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
46. Bossema, E.R., et al., Perioperative microembolism is not associated with cognitive outcome three months after carotid endarterectomy. European Journal of Vascular & Endovascular Surgery, 2005. 29(3): p. 262-8. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
47. Bowler, J.V. and P.B. Gorelick, Advances in vascular cognitive impairment. Stroke, 2009. 40(5): p. e315-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
48. BrÃ¦kken, S.K., et al., Association between intraoperative cerebral microembolic signals and postoperative neuropsychological deficit: Comparison between patients with cardiac valve replacement and patients with coronary artery bypass grafting. Journal of Neurology Neurosurgery and Psychiatry, 1998. 65(4): p. 573-576. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
49. Brand, N., et al., Left or right carotid endarterectomy in patients with atherosclerotic disease: ipsilateral effects on cognition? Brain & Cognition, 2004. 54(2): p. 117-23. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
50. Brillman, J., et al., Increased middle cerebral artery flow velocity during the initial phase of cardiopulmonary bypass may cause neurological dysfunction. Journal of Neuroimaging, 1995. 5(3): p. 135-41. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
51. Browndyke, J.N., et al., Acute neuropsychological functioning following cardiosurgical interventions associated with the production of intraoperative cerebral microemboli. Clinical Neuropsychologist, 2002. 16(4): p. 463-471. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
52. Browne, S.M., et al., Cognitive performance after cardiac operation: implications of regression toward the mean. Journal of Thoracic & Cardiovascular Surgery, 1999. 117(3): p. 481-5. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
53. Bruggemans, E.F., J.G. Van Dijk, and H.A. Huysmans, Residual cognitive dysfunctioning at 6 months following coronary artery bypass graft surgery. European Journal of Cardio-Thoracic Surgery, 1995. 9(11): p. 636-43. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
54. Bucerius, J., et al., Predictors of delirium after cardiac surgery delirium: Effect of beating-heart (off-pump) surgery. Journal of Thoracic and Cardiovascular Surgery, 2004. 127(1): p. 57-64. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
55. Bunch, T.J., et al., Patients treated with catheter ablation for atrial fibrillation have long-term rates of death, stroke, and dementia similar to patients without atrial fibrillation. Journal of Cardiovascular Electrophysiology, 2011. 22(8): p. 839-45. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
56. Burker, E.J., et al., The Mini Mental State Exam as a predictor of neuropsychological functioning after cardiac surgery. International Journal of Psychiatry in Medicine, 1995. 25(3): p. 263-76. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
57. Busch, T., et al., Combined approach for internal carotid artery stenosis and cardiovascular disease in septuagenarians--a comparative study. European Journal of Cardio-Thoracic Surgery, 1999. 16(6): p. 602-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
58. Buschbeck, D., et al., Short-term neuropsychologic differences after normothermic versus hypothermic cardiopulmonary bypass. Journal of Thoracic & Cardiovascular Surgery, 1998. 116(2): p. 350-3. POPULATION MEAN AGE <65
59. Butterworth, J., et al., Attempted control of hyperglycemia during cardiopulmonary bypass fails to improve neurologic or neurobehavioral outcomes in patients without diabetes mellitus undergoing coronary artery bypass grafting. Journal of Thoracic and Cardiovascular Surgery, 2005. 130(5): p. 1319.e1-1319.e9. POPULATION MEAN AGE <65
60. Buziashvili, Y.I., et al., Use of P300 cognitive evoked potentials in the diagnosis of impairments of higher mental functions after cardiac surgery in conditions of cardiopulmonary bypass. Neuroscience and Behavioral Physiology, 2006. 36(2): p. 115-118. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
61. Camboni, D., et al., Microbubble activity in miniaturized and in conventional extracorporeal circulation. ASAIO Journal, 2009. 55(1): p. 58-62. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
62. Capoccia, L., et al., Silent stroke and cognitive decline in asymptomatic carotid stenosis revascularization. Vascular, 2012. 20(4): p. 181-7. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)

63. Capoccia, L., et al., Comparative study on carotid revascularization (endarterectomy vs stenting) using markers of cellular brain injury, neuropsychometric tests, and diffusion-weighted magnetic resonance imaging. Journal of Vascular Surgery, 2010. 51(3): p. 584-91, 591.e1-3; discussion 592. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
64. Carroll, D.L., The importance of self-efficacy expectations in elderly patients recovering from coronary artery bypass surgery. Heart & Lung, 1995. 24(1): p. 50-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
65. Casey, C. and D.P. Faxon, Multi-vessel coronary disease percutaneous coronary intervention. Heart, 2004. 90(3): p. 341-346. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
66. Charlson, M.E., et al., Improvement of outcomes after coronary artery bypass II: a randomized trial comparing intraoperative high versus customized mean arterial pressure. Journal of Cardiac Surgery, 2007. 22(6): p. 465-72. POPULATION MEAN AGE <65
67. Chen, J., J. Yan, and X. Han, Dexmedetomidine may benefit cognitive function after laparoscopic cholecystectomy in elderly patients. Experimental and Therapeutic Medicine. 5(2): p. 489-494. NOT TREATED WITH CV PROCEDURE OF INTEREST
68. Cheng, D.C., et al., Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomized controlled trial. Journal of Thoracic & Cardiovascular Surgery, 1996. 112(3): p. 755-64. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
69. Chernov, V.I., et al., Short-term and long-term cognitive function and cerebral perfusion in off-pump and on-pump coronary artery bypass patients. European Journal of Cardio-thoracic Surgery, 2006. 29(1): p. 74-81. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
70. Chong, S.Y., et al., Deep hypothermic circulatory arrest in adults undergoing aortic surgery: Local experience. Annals of the Academy of Medicine Singapore, 2004. 33(3): p. 289-293. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
71. Chuang, Y.M., et al., Immediate regression of leukoaraiosis after carotid artery revascularization. Cerebrovascular Diseases. 32(5): p. 439-446. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
72. Cicekcioglu, F., et al., Neurocognitive functions after beating heart mitral valve replacement without cross-clamping the aorta. Journal of Cardiac Surgery, 2008. 23(2): p. 114-9. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
73. Clark, R.E., et al., Microemboli during coronary artery bypass grafting. Genesis and effect on outcome. Journal of Thoracic & Cardiovascular Surgery, 1995. 109(2): p. 249-57; discussion 257-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
74. Cook, D.J., et al., Postcardiac surgical cognitive impairment in the aged using diffusion-weighted magnetic resonance imaging. Annals of Thoracic Surgery, 2007. 83(4): p. 1389-95. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
75. Cormack F, Shipolini A, Awad WI, et al. A meta-analysis of cognitive outcome following coronary artery bypass graft surgery. Neurosci Biobehav Rev. 2012 Oct;36(9):2118-29. PMID: 22732162. POPULATION MEAN AGE <65
76. Czerny, M., et al., Sustained cognitive benefit 5 years after carotid endarterectomy. Journal of Vascular Surgery, 2010. 51(5): p. 1139-44. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
77. David Hillis, L., et al., 2011 ACCF/AHA guideline for coronary artery bypass graft surgery a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 124(23): p. e652-e735. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
78. de Tournay-Jette, E., et al., The relationship between cerebral oxygen saturation changes and postoperative cognitive dysfunction in elderly patients after coronary artery bypass graft surgery. Journal of Cardiothoracic & Vascular Anesthesia, 2011. 25(1): p. 95-104. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
79. de Tournay-Jette, E., et al., The benefits of cognitive training after a coronary artery bypass graft surgery. Journal of Behavioral Medicine, 2012. 35(5): p. 557-68. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
80. Deklunder, G., et al., Microemboli in cerebral circulation and alteration of cognitive abilities in patients with mechanical prosthetic heart valves. Stroke, 1998. 29(9): p. 1821-6. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
81. Detroyer, E., et al., Is preoperative anxiety and depression associated with onset of delirium after cardiac surgery in older patients? A prospective cohort study. J Am Geriatr Soc, 2008. 56(12): p. 2278-2284. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
82. Di Carlo, A., et al., Clinically relevant cognitive impairment after cardiac surgery: A 6-month follow-up study. J Neurol Sci, 2001. 188(1-2): p. 85-93. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL

83. Diegeler, A., et al., Neuromonitoring and neurocognitive outcome in off-pump versus conventional coronary bypass operation. Annals of Thoracic Surgery, 2000. 69(4): p. 1162-6. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
84. Dieleman, J., et al., Presence of coronary collaterals is associated with a decreased incidence of cognitive decline after coronary artery bypass surgery. European Journal of Cardio-Thoracic Surgery, 2009. 35(1): p. 48-53. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
85. DiMaria-Ghalili, R.A., Changes in nutritional status and postoperative outcomes in elderly CABG patients.[Erratum appears in Biol Res Nurs. 2004 Oct;6(2):158]. Biological Research for Nursing, 2002. 4(2): p. 73-84. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
86. DiSesa, V.J., Patient characteristics can predict improvement in functional health after elective coronary artery bypass grafting. Annals of Thoracic Surgery, 2003. 75(6): p. 1855. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
87. Djaiani, G.N., et al., Chronic exposure to nicotine does not prevent neurocognitive decline after cardiac surgery. Journal of Cardiothoracic & Vascular Anesthesia, 2003. 17(3): p. 341-5. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
88. Dogan, S., et al., Minimally invasive port access versus conventional mitral valve surgery: prospective randomized study. Annals of Thoracic Surgery, 2005. 79(2): p. 492-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
89. Dogan, S., et al., Minimally invasive versus conventional aortic valve replacement: a prospective randomized trial. Journal of Heart Valve Disease, 2003. 12(1): p. 76-80. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
90. Dogan, S., et al. How safe is the port access technique in minimally invasive coronary artery bypass grafting? The Annals of thoracic surgery, 2002. 74, 1537-43; discussion 1543. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
91. Doraiswamy, P.M., et al., Donepezil for cognitive decline following coronary artery bypass surgery: a pilot randomized controlled trial. Psychopharmacology Bulletin, 2007. 40(2): p. 54-62. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
92. Dowd, N.P., et al., Fast-track cardiac anaesthesia in the elderly: effect of two different anaesthetic techniques on mental recovery. British Journal of Anaesthesia, 2001. 86(1): p. 68-76. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
93. Dumas, A., et al., Early versus late extubation after coronary artery bypass grafting: effects on cognitive function. Journal of Cardiothoracic & Vascular Anesthesia, 1999. 13(2): p. 130-5. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
94. Dupuis, G., et al., Coronary artery bypass graft surgery and cognitive performance. American Journal of Critical Care, 2006. 15(5): p. 471-8; quiz 479. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
95. Ebert, A.D., et al., Early neurobehavioral disorders after cardiac surgery: a comparative analysis of coronary artery bypass graft surgery and valve replacement. Journal of Cardiothoracic & Vascular Anesthesia, 2001. 15(1): p. 15-9. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
96. Eifert, S., et al., Neurological and neuropsychological examination and outcome after use of an intra-aortic filter device during cardiac surgery. Perfusion, 2003. 18(SUPPL. 1): p. 55-60. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
97. Engelhardt, W., et al., Early cerebral functional outcome after coronary artery bypass surgery using different acid-base management during hypothermic cardiopulmonary bypass. Acta Anaesthesiologica Scandinavica, 1996. 40(4): p. 457-65. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
98. Engelman, R.M., et al. Is there a relationship between systemic perfusion temperature during coronary artery bypass grafting and extent of intraoperative ischemic central nervous system injury? The Journal of thoracic and cardiovascular surgery, 2000. 119, 230-2. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
99. Engelman, R.M., et al., Does cardiopulmonary bypass temperature correlate with postoperative central nervous system dysfunction? Journal of Cardiac Surgery, 1995. 10(4 Suppl): p. 493-7. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
100. Engelman, R.M., et al., Influence of cardiopulmonary bypass perfusion temperature on neurologic and hematologic function after coronary artery bypass grafting. Annals of Thoracic Surgery, 1999. 67(6): p. 1547-55; discussion 1556. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
101. Ernest, C.S., et al., Predictors of cognitive function in candidates for coronary artery bypass graft surgery. Journal of the International Neuropsychological Society, 2007. 13(2): p. 257-66. POPULATION MEAN AGE <65
102. Ernest, C.S., et al., Cognitive function in candidates for coronary artery bypass graft surgery. Annals of Thoracic Surgery, 2006. 82(3): p. 812-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL

103. Evered, L., et al., Postoperative cognitive dysfunction is independent of type of surgery and anesthetic. Anesthesia & Analgesia, 2011. 112(5): p. 1179-85. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
104. Fan, X.C., et al., Cognitive function in congenital heart disease after cardiac surgery with extracorporeal circulation. World Journal of Pediatrics. 6(3): p. 268-270. POPULATION MEAN AGE <65
105. Farsak, B., et al., Elevated levels of s-100Î² correlate with neurocognitive outcome after cardiac surgery. Journal of Cardiovascular Surgery, 2003. 44(1): p. 31-35. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
106. Fearn, S.J., et al., Carotid endarterectomy improves cognitive function in patients with exhausted cerebrovascular reserve. European Journal of Vascular & Endovascular Surgery, 2003. 26(5): p. 529-36. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
107. Fearn, S.J., et al., Cerebral injury during cardiopulmonary bypass: emboli impair memory. Journal of Thoracic & Cardiovascular Surgery, 2001. 121(6): p. 1150-60. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
108. Feliziani, F.T., et al., Cognitive performance in elderly patients undergoing carotid endarterectomy or carotid artery stenting: a twelve-month follow-up study. Cerebrovascular Diseases, 2010. 30(3): p. 244-51. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
109. Fiedler, J., et al., Cognitive outcome after EC-IC bypass surgery in hemodynamic cerebral ischemia. Acta Neurochirurgica. 153(6): p. 1303-1311. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
110. Floyd, T.F., et al., Clinically silent cerebral ischemic events after cardiac surgery: their incidence, regional vascular occurrence, and procedural dependence. Annals of Thoracic Surgery, 2006. 81(6): p. 2160-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
111. Fontanella, M., et al., Neuropsychological assessment after microsurgical clipping or endovascular treatment for anterior communicating artery aneurysm. Acta Neurochirurgica, 2003. 145(10): p. 867-872. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
112. Freedland, K.E., et al., Treatment of depression after coronary artery bypass surgery: a randomized controlled trial. Archives of General Psychiatry, 2009. 66(4): p. 387-96. POPULATION MEAN AGE <65
113. Friedlander, R. A study of the effects of minocycline on cognitive function after carotid endarterectomy. ClinicalTrials.gov, 2006. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
114. Fukunaga, S., et al., Neuropsychological changes in patients with carotid stenosis after carotid endarterectomy. European Neurology, 2006. 55(3): p. 145-50. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
115. Gallagher, R. and S. McKinley, Anxiety, depression and perceived control in patients having coronary artery bypass grafts. Journal of Advanced Nursing, 2009. 65(11): p. 2386-96. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
116. Gerriets, T., et al., Evaluation of methods to predict early long-term neurobehavioral outcome after coronary artery bypass grafting. American Journal of Cardiology, 2010. 105(8): p. 1095-101. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
117. Gerriets, T., et al., Protecting the brain from gaseous and solid micro-emboli during coronary artery bypass grafting: a randomized controlled trial. European Heart Journal, 2010. 31(3): p. 360-8. NO POST-PROCEDURE MEASURE OF COGNITION
118. Gold, J.P., et al., Improving outcomes in coronary surgery: the impact of echo-directed aortic cannulation and perioperative hemodynamic management in 500 patients. Annals of Thoracic Surgery, 2004. 78(5): p. 1579-85. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
119. Gossetti, B., et al., Embolism to the brain during carotid stenting and surgery. Acta Chirurgica Belgica, 2007. 107(2): p. 151-4. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
120. Goto, T., et al., Magnetic resonance imaging findings and postoperative neurologic dysfunction in elderly patients undergoing coronary artery bypass grafting. Annals of Thoracic Surgery, 2001. 72(1): p. 137-42. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
121. Goto, T., et al., Gender differences in stroke risk among the elderly after coronary artery surgery. Anesthesia and Analgesia, 2007. 104(5): p. 1016-1022. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
122. Gottesman, R.F., et al., Early postoperative cognitive dysfunction and blood pressure during coronary artery bypass graft operation. Archives of Neurology, 2007. 64(8): p. 1111-4. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
123. Gremigni, P., L. Sciarroni, and L. Pedrini, Cognitive changes after carotid endarterectomy. Monaldi Archives for Chest Disease, 2009. 72(2): p. 91-7. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
124. Grieco, G., et al., Evaluating neuroprotective agents for clinical anti-ischemic benefit using neurological and neuropsychological changes after cardiac surgery under cardiopulmonary bypass. Methodological strategies and results of a double-blind, placebo-controlled trial of GM1 ganglioside. Stroke, 1996. 27(5): p. 858-74. POPULATION MEAN AGE <65

125. Griffin, S., et al. The effect of substrate load and blood glucose management on cerebral dysfunction following cardiopulmonary bypass. Vasc Surg, 1992. 26, 656-664. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
126. Grigore, A.M., et al., The rewarming rate and increased peak temperature alter neurocognitive outcome after cardiac surgery. Anesthesia & Analgesia, 2002. 94(1): p. 4-10. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
127. Grigore, A.M., et al., Prospective randomized trial of normothermic versus hypothermic cardiopulmonary bypass on cognitive function after coronary artery bypass graft surgery. Anesthesiology, 2001. 95(5): p. 1110-9. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
128. Grimm, M., et al., Normothermic cardiopulmonary bypass is beneficial for cognitive brain function after coronary artery bypass grafting--a prospective randomized trial. European Journal of Cardio-Thoracic Surgery, 2000. 18(3): p. 270-5. POPULATION MEAN AGE <65
129. Grimm, M., et al., Neurocognitive deficit following mitral valve surgery. European Journal of Cardio-Thoracic Surgery, 2003. 23(3): p. 265-71. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
130. Gunaydin, B. and A. Babacan Cerebral hypoperfusion after cardiac surgery and anesthetic strategies: a comparative study with high dose fentanyl and barbiturate anesthesia. Annals of thoracic and cardiovascular surgery : official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia, 1998. 4, 12-7. POPULATION MEAN AGE <65
131. Haeusler, K.G., et al., 3 Tesla MRI-detected brain lesions after pulmonary vein isolation for atrial fibrillation: Results of the MACPAF study. J Cardiovasc Electrophysiol. 24(1): p. 14-21. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
132. Haeusler, K.G., et al., Stroke risk associated with balloon based catheter ablation for atrial fibrillation: Rationale and design of the MACPAF Study. BMC Neurology, 2010. 10: p. 63. POPULATION MEAN AGE <65
133. Haley, A.P., et al., Verbal working memory and atherosclerosis in patients with cardiovascular disease: An fMRI study. Journal of Neuroimaging, 2007. 17(3): p. 227-233. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
134. Hammon, J.W., et al., Single crossclamp improves 6-month cognitive outcome in high-risk coronary bypass patients: the effect of reduced aortic manipulation. Journal of Thoracic & Cardiovascular Surgery, 2006. 131(1): p. 114-21. POPULATION MEAN AGE <65
135. Hammon, J.W., et al., Coronary artery bypass grafting with single cross-clamp results in fewer persistent neuropsychological deficits than multiple clamp or off-pump coronary artery bypass grafting. Annals of Thoracic Surgery, 2007. 84(4): p. 1174-8; discussion 1178-9. POPULATION MEAN AGE <65
136. Harmon, D., et al., Plasma concentrations of nitric oxide products and cognitive dysfunction following coronary artery bypass surgery. European Journal of Anaesthesiology, 2005. 22(4): p. 269-76. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
137. Hegland, D., et al., Cerebral magnetic resonance findings in asymptomatic patients after atrial fibrillation catheter ablation: Cause for alarm or further study? J Cardiovasc Electrophysiol. 22(9): p. 969-972. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
138. Helgeson, V.S., Cognitive adaptation, psychological adjustment, and disease progression among angioplasty patients: 4 years later. Health Psychology, 2003. 22(1): p. 30-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
139. Henze, T., H. Stephan, and H. Sonntag, Cerebral dysfunction following extracorporeal circulation for aortocoronary bypass surgery: no differences in neuropsychological outcome after pulsatile versus nonpulsatile flow. Thoracic & Cardiovascular Surgeon, 1990. 38(2): p. 65-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
140. Hernandez, F., Jr., et al., Neurocognitive outcomes of off-pump versus on-pump coronary artery bypass: a prospective randomized controlled trial. Annals of Thoracic Surgery, 2007. 84(6): p. 1897-903. POPULATION MEAN AGE <65
141. Herrmann, M., et al., A contrastive analysis of release patterns of biochemical markers of brain damage after coronary artery bypass grafting and valve replacement and their association with the neurobehavioral outcome after cardiac surgery. European Journal of Cardio-Thoracic Surgery, 1999. 16(5): p. 513-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
142. Heyer, E.J., et al., Cerebral dysfunction after coronary artery bypass grafting done with mild or moderate hypothermia. Journal of Thoracic & Cardiovascular Surgery, 1997. 114(2): p. 270-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
143. Heyer, E.J., et al., Neuropsychometric changes in patients after carotid endarterectomy. Stroke, 1998. 29(6): p. 1110-5. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
144. Heyer, E.J., et al., A study of cognitive dysfunction in patients having carotid endarterectomy performed with regional anesthesia. Anesthesia & Analgesia, 2008. 107(2): p. 636-42. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE

145. Heyer, E.J., et al., Heparin-bonded cardiopulmonary bypass circuits reduce cognitive dysfunction. Journal of Cardiothoracic & Vascular Anesthesia, 2002. 16(1): p. 37-42. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
146. Heyer, E.J., et al., A controlled prospective study of neuropsychological dysfunction following carotid endarterectomy. Archives of Neurology, 2002. 59(2): p. 217-22. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
147. Heyer, E.J., et al., APOE-epsilon4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. Neurology, 2005. 65(11): p. 1759-63. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
148. Hickey, P.R., Neurologic sequelae associated with deep hypothermic circulatory arrest. Annals of Thoracic Surgery, 1998. 65(6 SUPPL.): p. S65-S70. POPULATION MEAN AGE <65
149. Hlatky, M.A., et al., Cognitive function 5 years after randomization to coronary angioplasty or coronary artery bypass graft surgery. Circulation, 1997. 96(9 Suppl): p. II-11-4; discussion II-15. POPULATION MEAN AGE <65
150. Ho, P.M., et al., Predictors of cognitive decline following coronary artery bypass graft surgery. Annals of Thoracic Surgery, 2004. 77(2): p. 597-603; discussion 603. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
151. Hogue, C.W., et al., Risk Factors for Neurocognitive Dysfunction After Cardiac Surgery in Postmenopausal Women. Annals of Thoracic Surgery, 2008. 86(2): p. 511-516. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
152. Huang, K.-L., et al., Impact of silent ischemic lesions on cognition following carotid artery stenting. European Neurology, 2011. 66(6): p. 351-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
153. Hudetz, J.A., et al., Postoperative delirium and short-term cognitive dysfunction occur more frequently in patients undergoing valve surgery with or without coronary artery bypass graft surgery compared with coronary artery bypass graft surgery alone: Results of a pilot study. J Cardiothorac Vasc Anesth. 25(5): p. 811-816. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
154. Hudetz, J.A., et al., Metabolic syndrome exacerbates short-term postoperative cognitive dysfunction in patients undergoing cardiac surgery: Results of a pilot study. Journal of Cardiothoracic and Vascular Anesthesia. 25(2): p. 282-287. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
155. Hudetz, J.A., K.M. Patterson, and P.S. Pagel, Comparison of pre-existing cognitive impairment, amnesic mild cognitive impairment, and multiple domain mild cognitive impairment in men scheduled for coronary artery surgery. European Journal of Anaesthesiology, 2012. 29(7): p. 320-5. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
156. Isgro, F., et al., A predictive parameter in patients with brain related complications after cardiac surgery? European Journal of Cardio-Thoracic Surgery, 1997. 11(4): p. 640-4. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
157. Ishihara, H., et al., Cognitive outcome differences on the side of carotid artery stenting. Journal of Vascular Surgery, 2013. 57(1): p. 125-30. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
158. Iskesen, I., et al., Opening the cardiac chambers does not make any difference in p300 measurement. Heart Surgery Forum, 2006. 9(5): p. E770-3. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
159. Jansen, C., et al. Cognitive functions after surgery or stenting in extracranial stenosis of the carotid artery. Stroke, 2009. 40, e175. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
160. Johnston, S.C., et al., Cognitive impairment and decline are associated with carotid artery disease in patients without clinically evident cerebrovascular disease. Annals of Internal Medicine, 2004. 140(4): p. 237-47. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
161. Kadoi, Y. and F. Goto, Factors associated with postoperative cognitive dysfunction in patients undergoing cardiac surgery. Surgery Today, 2006. 36(12): p. 1053-7. POPULATION MEAN AGE <65
162. Kadoi Y, Saito S, Fujita N, et al. Effects of balloon-induced pulsatile perfusion on postoperative short- and long-term cognitive dysfunction in diabetic patients with impaired cerebrovascular carbon dioxide reactivity. J Cardiothorac Vasc Anesth. 2013 Apr;27(2):238-44. PMID: 23063103. POPULATION MEAN AGE <65
163. Kadoi, Y., et al., Slow rewarming has no effects on the decrease in jugular venous oxygen hemoglobin saturation and long-term cognitive outcome in diabetic patients. Anesthesia & Analgesia, 2002. 94(6): p. 1395-401, table of contents. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
164. Kadoi, Y., et al., Jugular venous oxygen saturation during mild hypothermic versus normothermic cardiopulmonary bypass in elderly patients. Surgery Today, 2004. 34(5): p. 399-404. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE

165. Kahlert, P., et al., Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation: A diffusion-weighted magnetic resonance imaging study. Circulation. 121(7): p. 870-878. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
166. Kapetanakis, E.I., et al., The impact of aortic manipulation on neurologic outcomes after coronary artery bypass surgery: a risk-adjusted study. Annals of Thoracic Surgery, 2004. 78(5): p. 1564-71. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
167. Kapetanakis, E.I., et al., Comparison of the quality of life after conventional versus off-pump coronary artery bypass surgery. Journal of Cardiac Surgery, 2008. 23(2): p. 120-5. NO POST-PROCEDURE MEASURE OF COGNITION
168. Kapur, A., et al., The Coronary Artery Revascularisation in Diabetes (CARDia) trial: Background, aims, and design. American Heart Journal, 2005. 149(1): p. 13-19. NO POST-PROCEDURE MEASURE OF COGNITION
169. Karhunen, J.P., et al., Long-term survival and quality of life after cardiac resuscitation following coronary artery bypass grafting. European Journal of Cardio-Thoracic Surgery, 2011. 40(1): p. 249-54. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
170. Kassaian, S.E., et al., A novel scoring system for identifying high-risk patients undergiong carotid stenting. Archives of Iranian Medicine, 2006. 9(2): p. 129-137. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
171. Kaukinen, L., et al., Release of brain-specific creatine kinase and neuron-specific enolase into cerebrospinal fluid after hypothermic and normothermic cardiopulmonary bypass in coronary artery surgery. Acta Anaesthesiologica Scandinavica, 2000. 44(4): p. 361-8. POPULATION MEAN AGE <65
172. Kaukuntla, H., et al., Differential brain and body temperature during cardiopulmonary bypass--a randomised clinical study. European Journal of Cardio-Thoracic Surgery, 2004. 26(3): p. 571-9. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
173. Kazmierski, J., et al., Preoperative predictors of delirium after cardiac surgery: a preliminary study. General Hospital Psychiatry, 2006. 28(6): p. 536-538. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
174. Keary, T.A., et al., Blood pressure variability and dementia rating scale performance in older adults with cardiovascular disease. Cognitive and Behavioral Neurology, 2007. 20(1): p. 73-77. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
175. Keizer, A.M.A., et al., Cognitive self-assessment one year after on-pump and off-pump coronary artery bypass grafting. Annals of Thoracic Surgery, 2003. 75(3): p. 835-8; discussion 838-9. POPULATION MEAN AGE <65
176. Kennedy ED, Choy KC, Alston RP, et al. Cognitive outcome after on- and off-pump coronary artery bypass grafting surgery: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth. 2013 Apr;27(2):253-65. PMID: 23507014. POPULATION MEAN AGE <65
177. Kervan, U., et al., Comparison of neurocognitive functions after beating-heart mitral valve replacement without aorta cross-clamping and after standard mitral valve replacement with cardioplegic arrest. Heart Surgery Forum. 14(6): p. E335-E339. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
178. Khosravi, A., et al., Evaluation of coated oxygenators in cardiopulmonary-bypass systems and their impact on neurocognitive function. Perfusion, 2005. 20(5): p. 249-54. POPULATION MEAN AGE <65
179. Khoueiry, G., et al., Depression, disability, and quality of life after off-pump coronary artery bypass grafting: a prospective 9-month follow-up study. Heart & Lung, 2011. 40(3): p. 217-25. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
180. Kilminster, S., et al., Neuropsychological change and S-100 protein release in 130 unselected patients undergoing cardiac surgery. Stroke, 1999. 30(9): p. 1869-1874. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
181. Kilo, J., et al., Cardiopulmonary bypass affects cognitive brain function after coronary artery bypass grafting. Annals of Thoracic Surgery, 2001. 72(6): p. 1926-32. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
182. Knipp, S.C., et al., Small ischemic brain lesions after cardiac valve replacement detected by diffusion-weighted magnetic resonance imaging: relation to neurocognitive function. European Journal of Cardio-Thoracic Surgery, 2005. 28(1): p. 88-96. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
183. Knipp, S.C., et al., Cognitive outcomes three years after coronary artery bypass surgery: relation to diffusion-weighted magnetic resonance imaging. Annals of Thoracic Surgery, 2008. 85(3): p. 872-9. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
184. Knopman, D.S., et al., Coronary artery bypass grafting is not a risk factor for dementia or Alzheimer disease. Neurology, 2005. 65(7): p. 986-90. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
185. Kobayashi, J., et al., Early outcome of a randomized comparison of off-pump and on-pump multiple arterial coronary revascularization. Circulation, 2005. 112(9 Suppl): p. I338-43. NO POST-PROCEDURE MEASURE OF COGNITION

186. Komotar, R.J., E.J. Heyer, and E.S. Connolly Jr, Cognitive outcomes after carotid revascularization: The role of cerebral emboli and hypoperfusion - Commentary. Neurosurgery, 2008. 62(2): p. 393-394. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
187. Kozora, E., et al., Cognitive outcomes after on- versus off-pump coronary artery bypass surgery. Annals of Thoracic Surgery, 2010. 90(4): p. 1134-41. POPULATION MEAN AGE <65
188. Krone, R.J., et al., Ad hoc percutaneous coronary interventions in patients with stable coronary artery disease--a study of prevalence, safety, and variation in use from the American College of Cardiology National Cardiovascular Data Registry (ACC-NCDR). Catheterization & Cardiovascular Interventions, 2006. 68(5): p. 696-703. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
189. Kumar, R.A., et al., Predictive value of IL-18 and SC5b-9 for neurocognitive dysfunction after cardiopulmonary bypass. British Journal of Anaesthesia, 2007. 98(3): p. 317-22. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
190. Lal, B.K., et al., Cognitive changes after surgery vs stenting for carotid artery stenosis. Journal of Vascular Surgery, 2011. 54(3): p. 691-8. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
191. Lamy, A., et al., Rationale and design of the coronary artery bypass grafting surgery off or on pump revascularization study: A large international randomized trial in cardiac surgery. Am Heart J. 163(1): p. 1-6. NO POST-PROCEDURE MEASURE OF COGNITION
192. Lazibat, I., et al., Predictors of short-term neurocognitive outcome following coronary revascularisation (CABG) depending on the use of cardiopulmonary bypass. Collegium Antropologicum, 2012. 36(3): p. 827-33. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
193. Lee, G.A., Determinants of quality of life five years after coronary artery bypass graft surgery. Heart & Lung, 2009. 38(2): p. 91-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
194. Lee, T.A., et al., Assessment of the emergence of Alzheimer's disease following coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty. Journal of Alzheimer's Disease, 2005. 7(4): p. 319-24. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
195. Lee, W.H., et al. Effects of extracorporeal circulation upon behavior, personality, and brain function. II. Hemodynamic, metabolic, and psychometric correlations. Annals of surgery, 1971. 173, 1013-23. POPULATION MEAN AGE <65
196. Lelis, R.G.B., et al., Apolipoprotein E4 genotype increases the risk of postoperative cognitive dysfunction in patients undergoing coronary artery bypass graft surgery. Journal of Cardiovascular Surgery, 2006. 47(4): p. 451-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
197. Lewis, M.S., et al., Detection of postoperative cognitive decline after coronary artery bypass graft surgery is affected by the number of neuropsychological tests in the assessment battery. Annals of Thoracic Surgery, 2006. 81(6): p. 2097-104. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
198. Lewis, M.S., et al., The sensitivity and specificity of three common statistical rules for the classification of post-operative cognitive dysfunction following coronary artery bypass graft surgery. Acta Anaesthesiologica Scandinavica, 2006. 50(1): p. 50-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
199. Lewis, M.S., et al., The influence of different error estimates in the detection of postoperative cognitive dysfunction using reliable change indices with correction for practice effects.[Republished from Arch Clin Neuropsychol. 2006 Aug;21(5):421-7; PMID: 16859888]. Archives of Clinical Neuropsychology, 2007. 22(2): p. 249-57. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
200. Lewis, M.S., P.T. Maruff, and B.S. Silbert, Examination of the use of cognitive domains in postoperative cognitive dysfunction after coronary artery bypass graft surgery. Annals of Thoracic Surgery, 2005. 80(3): p. 910-6. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
201. Lin, M.-S., et al., Neurocognitive improvement after carotid artery stenting in patients with chronic internal carotid artery occlusion and cerebral ischemia. Stroke, 2011. 42(10): p. 2850-4. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
202. Lindsay, G.M., et al., Assessment of changes in general health status using the short-form 36 questionnaire 1 year following coronary artery bypass grafting. European Journal of Cardio-Thoracic Surgery, 2000. 18(5): p. 557-64. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
203. Liu, Y.-H., et al., The effects of cardiopulmonary bypass on the number of cerebral microemboli and the incidence of cognitive dysfunction after coronary artery bypass graft surgery. Anesthesia & Analgesia, 2009. 109(4): p. 1013-22. POPULATION MEAN AGE <65
204. Lloyd, A.J., et al., Does carotid endarterectomy lead to a decline in cognitive function or health related quality of life? Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society, 2004. 26(6): p. 817-25. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST

205. Lloyd, C.T., et al., Serum S-100 protein release and neuropsychologic outcome during coronary revascularization on the beating heart: a prospective randomized study. Journal of Thoracic & Cardiovascular Surgery, 2000. 119(1): p. 148-54. POPULATION MEAN AGE <65
206. Lund, C., et al., Comparison of cerebral embolization during off-pump and on-pump coronary artery bypass surgery. Annals of Thoracic Surgery, 2003. 76(3): p. 765-70; discussion 770. POPULATION MEAN AGE <65
207. Lyketsos, C.G., et al., A population-based study of the association between coronary artery bypass graft surgery (CABG) and cognitive decline: the Cache County study. International Journal of Geriatric Psychiatry, 2006. 21(6): p. 509-18. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
208. Maekawa, K., et al., Impaired cognition preceding cardiac surgery is related to cerebral ischemic lesions. Journal of Anesthesia. 25(3): p. 330-336. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
209. Mahanna, E.P., et al., Defining neuropsychological dysfunction after coronary artery bypass grafting. Annals of Thoracic Surgery, 1996. 61(5): p. 1342-7. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
210. Maldonado, J.R., et al., Dexmedetomidine and the reduction of postoperative delirium after cardiac surgery. Psychosomatics, 2009. 50(3): p. 206-17. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
211. Malheiros, S.M., et al., Neurological outcome in coronary artery surgery with and without cardiopulmonary bypass. Acta Neurologica Scandinavica, 1995. 92(3): p. 256-60. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
212. Mariani, M.A., A. D'Alfonso, and J.G. Grandjean, Total arterial off-pump coronary surgery: time to change our habits? Annals of Thoracic Surgery, 2004. 78(5): p. 1591-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
213. Maron, D.J., et al., Intensive Multifactorial Intervention for Stable Coronary Artery Disease. Optimal Medical Therapy in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) Trial. J Am Coll Cardiol. 55(13): p. 1348-1358. POPULATION MEAN AGE <65
214. Martens, S., et al., Conventional carbon dioxide application does not reduce cerebral or myocardial damage in open heart surgery. Annals of Thoracic Surgery, 2001. 72(6): p. 1940-1944. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
215. Mathew, J.P., et al., A Multicenter Risk Index for Atrial Fibrillation after Cardiac Surgery. Journal of the American Medical Association, 2004. 291(14): p. 1720-1729. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
216. Mathew, J.P., et al. Effects of extreme hemodilution during cardiac surgery on cognitive function in the elderly. Anesthesiology, 2007. 107, 577-84 DOI: 10.1097/01.anes.0000281896.07256.71. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
217. Mathew, J.P., et al., Genetic variants in P-selectin and C-reactive protein influence susceptibility to cognitive decline after cardiac surgery. Journal of the American College of Cardiology, 2007. 49(19): p. 1934-42. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
218. Mathisen, L., et al., Changes in cardiac and cognitive function and self-reported outcomes at one year after coronary artery bypass grafting. Journal of Thoracic & Cardiovascular Surgery, 2010. 140(1): p. 122-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
219. Mattlar, C.E., et al., The proportion of patients with cognitive impairment after coronary artery bypass surgery: an 8-month follow-up study. Psychotherapy & Psychosomatics, 1991. 55(2-4): p. 145-50. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
220. McKhann, G.M., et al., Depression and cognitive decline after coronary artery bypass grafting. Lancet, 1997. 349(9061): p. 1282-4. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
221. McKhann, G.M., et al., Cognitive outcome after coronary artery bypass: a one-year prospective study. Annals of Thoracic Surgery, 1997. 63(2): p. 510-5. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
222. McKhann, G.M., et al., Subjective memory symptoms in surgical and nonsurgical coronary artery patients: 6-year follow-up. Annals of Thoracic Surgery, 2009. 87(1): p. 27-34. POPULATION MEAN AGE <65
223. McLean, R.F., et al., Cardiopulmonary bypass, temperature, and central nervous system dysfunction. Circulation, 1994. 90(5 Pt 2): p. II250-5. POPULATION MEAN AGE <65
224. Meyer, J.S., et al. Effects of medical and surgical treatment on cerebral perfusion and cognition in patients with chronic cerebral ischemia. Surgical neurology, 1990. 34, 301-8. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
225. Mielke, M.M., et al., Vascular factors predict rate of progression in Alzheimer disease. Neurology, 2007. 69(19): p. 1850-8. NOT TREATED WITH CV PROCEDURE OF INTEREST

226. Millar, K., A.J. Asbury, and G.D. Murray, Pre-existing cognitive impairment as a factor influencing outcome after cardiac surgery. British Journal of Anaesthesia, 2001. 86(1): p. 63-7. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
227. Mirow, N., et al., Diffusion-weighted magnetic resonance imaging for the detection of ischemic brain lesions in coronary artery bypass graft surgery: relation to extracorporeal circulation and heparinization. Journal of Cardiovascular Surgery, 2011. 52(1): p. 117-26. NO POST-PROCEDURE MEASURE OF COGNITION
228. Mitchell, S.J., et al., Cerebral protection by lidocaine during cardiac operations: a follow-up study. Annals of Thoracic Surgery, 2009. 87(3): p. 820-5. POPULATION MEAN AGE <65
229. Miyanaga, S., et al. Impact of pulmonary vein isolation on the autonomic modulation in patients with paroxysmal atrial fibrillation and prolonged sinus pauses. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology, 2009. 11, 576-81 DOI: 10.1093/europace/eup082. NO POST-PROCEDURE MEASURE OF COGNITION
230. Mlekusch, W., et al., Improvement of neurocognitive function after protected carotid artery stenting. Catheterization & Cardiovascular Interventions, 2008. 71(1): p. 114-9. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
231. Mocco, J., et al., Galbraith Award: evaluation of risk factors associated with neurocognitive changes after carotid endarterectomy. Clinical Neurosurgery, 2006. 53: p. 301-6. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
232. Mongero, L.B., et al., Cardiac surgical patients exposed to heparin-bonded circuits develop less postoperative cerebral dysfunction than patients exposed to non-heparin-bonded circuits. Perfusion, 2001. 16(2): p. 107-11. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
233. Mononen, H., M. Lepojarvi, and T. Kallanranta, Early neuropsychological outcome after carotid endarterectomy. European Neurology, 1990. 30(6): p. 328-33. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
234. Mora, C.T., et al., The effect of temperature management during cardiopulmonary bypass on neurologic and neuropsychologic outcomes in patients undergoing coronary revascularization. Journal of Thoracic & Cardiovascular Surgery, 1996. 112(2): p. 514-22. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
235. Moraca, R., et al., Impaired baseline regional cerebral perfusion in patients referred for coronary artery bypass. Journal of Thoracic & Cardiovascular Surgery, 2006. 131(3): p. 540-6. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
236. Moran, S.M., et al., Prediction of survival by the Clifton Assessment Procedures for the Elderly (CAPE). British Journal of Clinical Psychology, 1990. 29(Pt 2): p. 225-6. NOT TREATED WITH CV PROCEDURE OF INTEREST
237. Mortensen, O.S., et al., Health related quality of life after conservative or invasive treatment of inducible postinfarction ischaemia. DANAMI study group. Heart, 2000. 84(5): p. 535-40. POPULATION MEAN AGE <65
238. Moser, D.J., et al., Neuropsychological performance is associated with vascular function in patients with atherosclerotic vascular disease. Arteriosclerosis, Thrombosis, and Vascular Biology, 2007. 27(1): p. 141-146. NOT TREATED WITH CV PROCEDURE OF INTEREST
239. Motallebzadeh, R., et al., Neurocognitive function and cerebral emboli: randomized study of on-pump versus off-pump coronary artery bypass surgery. Annals of Thoracic Surgery, 2007. 83(2): p. 475-82. POPULATION MEAN AGE <65
240. Mracek, J., et al., The impact of general versus local anesthesia on early subclinical cognitive function following carotid endarterectomy evaluated using P3 event-related potentials. Acta Neurochirurgica, 2012. 154(3): p. 433-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
241. Mullges, W., et al., Cognitive performance after coronary artery bypass grafting: a follow-up study. Neurology, 2002. 59(5): p. 741-3. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
242. Mullges, W., et al., Early natural course of transient encephalopathy after coronary artery bypass grafting. Critical Care Medicine, 2000. 28(6): p. 1808-11. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
243. Mullges, W., et al., Reduced rate of microembolism by optimized aortic cannula position does not influence early postoperative cognitive performance in CABG patients. Cerebrovascular Diseases, 2003. 15(3): p. 192-8. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
244. Murata, K., et al., Cognitive alteration after carotid revascularization is correlated with cortical GABA B-ergic modulations. Neuroscience Letters. 500(3): p. 151-156. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST

245. Murkin, J.M., et al., A randomized study of the influence of perfusion technique and pH management strategy in 316 patients undergoing coronary artery bypass surgery. II. Neurologic and cognitive outcomes. Journal of Thoracic & Cardiovascular Surgery, 1995. 110(2): p. 349-62. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
246. Musumeci, F., et al. Prospective randomized trial of single clamp technique versus intermittent ischaemic arrest: myocardial and neurological outcome. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, 1998. 13, 702-9. POPULATION MEAN AGE <65
247. Mutch, W.A.C., et al., Dementia and depression with ischemic heart disease: a population-based longitudinal study comparing interventional approaches to medical management. PLoS ONE [Electronic Resource], 2011. 6(2): p. e17457. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
248. Nadareishvili, Z.G., et al., Is cerebral microembolism in mechanical prosthetic heart valves clinically relevant? Journal of Neuroimaging, 2002. 12(4): p. 310-5. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
249. Nathan, H.J., et al., The management of temperature during cardiopulmonary bypass: Effect on neuropsychological outcome. Journal of Cardiac Surgery, 1995. 10(4 SUPPL.): p. 481-487. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
250. Neville, M.J., et al., Similar neurobehavioral outcome after valve or coronary artery operations despite differing carotid embolic counts. Journal of Thoracic & Cardiovascular Surgery, 2001. 121(1): p. 125-36. POPULATION MEAN AGE <65
251. Newman, M.F., et al., Effect of aging on cerebral autoregulation during cardiopulmonary bypass. Association with postoperative cognitive dysfunction. Circulation, 1994. 90(5 Pt 2): p. II243-9. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
252. Newman, M.F., et al., Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery.[Erratum appears in N Engl J Med 2001 Jun 14;344(24):1876]. New England Journal of Medicine, 2001. 344(6): p. 395-402. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
253. Nilsson, J., et al., A randomized study of coronary artery bypass surgery performed with the Resting Heartâ„¢ System utilizing a low vs a standard dosage of heparin. Interact Cardiovasc Thorac Surg. 2012 15(5): p. 834-839. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
254. Novitzky, D., et al., A study design to assess the safety and efficacy of on-pump versus off-pump coronary bypass grafting: the ROOBY trial. Clinical Trials, 2007. 4(1): p. 81-91. NO POST-PROCEDURE MEASURE OF COGNITION
255. Nussmeier, N.A., et al., Predictive value of the National Institutes of Health Stroke Scale and the Mini-Mental State Examination for neurologic outcome after coronary artery bypass graft surgery. Journal of Thoracic & Cardiovascular Surgery, 2010. 139(4): p. 901-12. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
256. Oden, K.E., C.G. Kevorkian, and J.K. Levy, Rehabilitation of the post-cardiac surgery stroke patient: analysis of cognitive and functional assessment. Archives of Physical Medicine & Rehabilitation, 1998. 79(1): p. 67-71. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
257. Ogasawara, K., et al., Postoperative cerebral hyperperfusion associated with impaired cognitive function in patients undergoing carotid endarterectomy. Journal of Neurosurgery, 2005. 102(1): p. 38-44. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
258. Oh, Y.J., et al., Diabetes mellitus does not affect jugular bulb oxygen saturation in patients undergoing off-pump coronary artery bypass graft surgery. Circulation Journal, 2008. 72(8): p. 1259-64. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
259. Okita, Y., et al., Prospective comparative study of brain protection in total aortic arch replacement: Deep hypothermic circulatory arrest with retrograde cerebral perfusion or selective antegrade cerebral perfusion. Annals of Thoracic Surgery, 2001. 72(1): p. 72-79. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
260. Okonkwo, O.C., et al., Longitudinal trajectories of cognitive decline among older adults with cardiovascular disease. Cerebrovascular Diseases, 2010. 30(4): p. 362-73. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
261. Oprisiu-Fournier, R., et al., AT1 receptor blockers for cognition decline after cardiac surgery? [13]. Stroke, 2006. 37(11): p. 2666. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
262. Orne, R.M.L.E. and L. Balacumaraswami, Benefits of off-pump coronary artery surgery? Anaesthesia, 2003. 58(5): p. 481-482. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
263. Ortega G, Alvarez B, Quintana M, et al. Cognitive improvement in patients with severe carotid artery stenosis after transcervical stenting with protective flow reversal. Cerebrovasc Dis. 2013;35(2):124-30. PMID: 23406878. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST

264. Pacini, D., et al., Cerebral functions and metabolism after antegrade selective cerebral perfusion in aortic arch surgery. European Journal of Cardio-Thoracic Surgery, 2010. 37(6): p. 1322-31. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
265. Palombo, D., et al., Subtle cerebral damage after shunting vs non shunting during carotid endarterectomy. European Journal of Vascular & Endovascular Surgery, 2007. 34(5): p. 546-51. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
266. Palotas, A., et al., Coronary artery bypass surgery provokes Alzheimer's disease-like changes in the cerebrospinal fluid. Journal of Alzheimer's Disease, 2010. 21(4): p. 1153-64. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
267. Panagopoulou, E., A. Montgomery, and A. Benos, Quality of life after coronary artery bypass grafting: evaluating the influence of preoperative physical and psychosocial functioning. Journal of Psychosomatic Research, 2006. 60(6): p. 639-44. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
268. Panday, G.F.V., et al., Minimal extracorporeal circulation and off-pump compared to conventional cardiopulmonary bypass in coronary surgery. Interactive Cardiovascular & Thoracic Surgery, 2009. 9(5): p. 832-6. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
269. Pandit, J.J. and D. Pigott, Cognitive dysfunction after cardiac surgery: Strategies for prevention. British Journal of Cardiology, 2001. 8(11): p. 613-616. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
270. Patel, D., et al., Long-term functional and neurocognitive recovery in patients who had an acute cerebrovascular event secondary to catheter ablation for atrial fibrillation. Journal of Cardiovascular Electrophysiology, 2010. 21(4): p. 412-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
271. Patel, R.L., et al., Alpha-stat acid-base regulation during cardiopulmonary bypass improves neuropsychologic outcome in patients undergoing coronary artery bypass grafting. Journal of Thoracic & Cardiovascular Surgery, 1996. 111(6): p. 1267-79. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
272. Patel, R.L., et al., Hyperperfusion and cerebral dysfunction. Effect of differing acid-base management during cardiopulmonary bypass. European Journal of Cardio-Thoracic Surgery, 1993. 7(9): p. 457-63; discussion 464. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
273. Pearson, S., G. Maddern, and R. Fitridge, Cognitive performance in patients after carotid endarterectomy. Journal of Vascular Surgery, 2003. 38(6): p. 1248-52; discussion 1252-3. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
274. Petrovitch, H., et al., Influence of myocardial infarction, coronary artery bypass surgery, and stroke on cognitive impairment in late life. American Journal of Cardiology, 1998. 81(8): p. 1017-21. NOT TREATED WITH CV PROCEDURE OF INTEREST
275. Petrucci, R.J., Finding our way from the heart to the head. Journal of Thoracic and Cardiovascular Surgery, 2003. 126(4): p. 944-946. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
276. Pettigrew, L.C., et al., Low mini-mental status predicts mortality in asymptomatic carotid arterial stenosis. Asymptomatic Carotid Atherosclerosis Study investigators. Neurology, 2000. 55(1): p. 30-4. NO POST-PROCEDURE MEASURE OF COGNITION
277. Phillips Bute, B., et al., Female gender is associated with impaired quality of life 1 year after coronary artery bypass surgery. Psychosomatic Medicine, 2003. 65(6): p. 944-51. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
278. Pirraglia, P.A., et al. The efficacy and safety of a pharmacologic protocol for maintaining coronary artery bypass patients at a higher mean arterial pressure during cardiopulmonary bypass. The Journal of extra-corporeal technology, 1998. 30, 64-72. NO POST-PROCEDURE MEASURE OF COGNITION
279. Potter, G.G., et al., Age effects of coronary artery bypass graft on cognitive status change among elderly male twins. Neurology, 2004. 63(12): p. 2245-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
280. Prapas, S.N., et al. Female risk using OPCAB, pi-circuit, and aorta no-touch coronary revascularization. The heart surgery forum, 2009. 12, E344-8 DOI: 10.1532/HSF98.20091124. NO POST-PROCEDURE MEASURE OF COGNITION
281. Prapas, S.N., et al., Aorta no-touch off-pump coronary artery revascularization in octogenarians: 5 Years' experience. Heart Surgery Forum, 2009. 12(6): p. E349-E353. NO POST-PROCEDURE MEASURE OF COGNITION
282. Proust, F., et al., Quality of life and brain damage after microsurgical clip occlusion or endovascular coil embolization for ruptured anterior communicating artery aneurysms: Neuropsychological assessment - Clinical article. Journal of Neurosurgery, 2009. 110(1): p. 19-29. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)

283. Puskas, F., et al., Intraoperative hyperglycemia and cognitive decline after CABG. Annals of Thoracic Surgery, 2007. 84(5): p. 1467-73. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
284. Puskas, J.D., et al., Neurocognitive and neuroanatomic changes after off-pump versus on-pump coronary artery bypass grafting: long-term follow-up of a randomized trial. Journal of Thoracic & Cardiovascular Surgery, 2011. 141(5): p. 1116-27. POPULATION MEAN AGE <65
285. Raabe, R.D., R.B. Burr, and R. Short, One-year Cognitive Outcomes Associated with Carotid Artery Stent Placement. Journal of Vascular and Interventional Radiology. 21(7): p. 983-988. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
286. Rabee, H.M., et al., Neurobehavioral effects of carotid endarterectomy. Saudi Medical Journal, 2001. 22(5): p. 433-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
287. Ramlawi, B., et al., Serologic markers of brain injury and cognitive function after cardiopulmonary bypass. Annals of Surgery, 2006. 244(4): p. 593-601. NO POST-PROCEDURE MEASURE OF COGNITION
288. Rankin, K.P., et al., Presurgical cognitive deficits in patients receiving coronary artery bypass graft surgery. Journal of the International Neuropsychological Society, 2003. 9(6): p. 913-24. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
289. Rasmussen, L.S., et al., Do blood levels of neuron-specific enolase and S-100 protein reflect cognitive dysfunction after coronary artery bypass? Acta Anaesthesiologica Scandinavica, 1999. 43(5): p. 495-500. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
290. Rasmussen, L.S., et al., Subtle brain damage cannot be detected by measuring neuron-specific enolase and S-100beta protein after carotid endarterectomy. Journal of Cardiothoracic & Vascular Anesthesia, 2000. 14(2): p. 166-70. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
291. Raymond, P.D., et al., Assessment of statistical change criteria used to define significant change in neuropsychological test performance following cardiac surgery. European Journal of Cardio-Thoracic Surgery, 2006. 29(1): p. 82-8. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
292. Reents, W., et al. Reduction of cerebral microemboli by positioning the aortic cannula in the descending aorta. Kardiotechnik, 2002. 11, 41-44. FULL TEXT UNAVAILABLE
293. Regragui, I., et al., The effects of cardiopulmonary bypass temperature on neuropsychologic outcome after coronary artery operations: a prospective randomized trial. Journal of Thoracic & Cardiovascular Surgery, 1996. 112(4): p. 1036-45. POPULATION MEAN AGE <65
294. Reich, D.L., et al., Using jugular bulb oxyhemoglobin saturation to guide onset of deep hypothermic circulatory arrest does not affect post-operative neuropsychological function. European Journal of Cardio-Thoracic Surgery, 2004. 25(3): p. 401-406. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
295. Reis, H.J., et al., Different inflammatory biomarker patterns in the cerebro-spinal fluid following heart surgery and major non-cardiac operations. Current Drug Metabolism, 2007. 8(6): p. 639-42. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
296. Restrepo, L., et al., Diffusion- and perfusion-weighted magnetic resonance imaging of the brain before and after coronary artery bypass grafting surgery. Stroke, 2002. 33(12): p. 2909-15. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
297. Rimington, H., J. Weinman, and J.B. Chambers, Predicting outcome after valve replacement. Heart, 2010. 96(2): p. 118-23. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
298. Roach, G.W., et al., Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. New England Journal of Medicine, 1996. 335(25): p. 1857-63. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
299. Roberts, R.O., et al., Coronary heart disease is associated with non-amnestic mild cognitive impairment. Neurobiology of Aging, 2010. 31(11): p. 1894-902. NOT TREATED WITH CV PROCEDURE OF INTEREST
300. Robson, M.J., et al., Cognition after coronary artery surgery is not related to postoperative jugular bulb oxyhemoglobin desaturation. Anesthesia & Analgesia, 2000. 91(6): p. 1317-26. POPULATION MEAN AGE <65
301. Rodes-Cabau, J., et al., Cerebral embolism following transcatheter aortic valve implantation: comparison of transfemoral and transapical approaches. Journal of the American College of Cardiology, 2011. 57(1): p. 18-28. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
302. Rodig, G., et al., Evaluation of self-reported failures in cognitive function after cardiac and noncardiac surgery. Anaesthesia, 1999. 54(9): p. 826-30. FULL TEXT UNAVAILABLE; NOT IN ENGLISH

303. Rodig, G. and K. Taeger Memory function in the early postoperative period after cardiac surgery - Impact of the anaesthetic procedure and comparison with memory function after vascular surgery. Anasthesiologie und Intensivmedizin, 2002. 43, 431-455. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
304. Rodriguez, R.A., et al., Cerebral emboli detected by transcranial Doppler during cardiopulmonary bypass are not correlated with postoperative cognitive deficits. Stroke, 2010. 41(10): p. 2229-35. POPULATION MEAN AGE <65
305. Rollman, B.L. and B.H. Belnap, The Bypassing the Blues trial: collaborative care for post-CABG depression and implications for future research. Cleveland Clinic Journal of Medicine, 2011. 78 Suppl 1: p. S4-12. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
306. Roman, P.E.F. and A.M. Grigore, Pro: Hypothermic cardiopulmonary bypass should be used routinely. J Cardiothorac Vasc Anesth. 26(5): p. 945-948. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
307. Ropacki, S.A., et al., The influence of cognitive reserve on neuropsychological functioning following coronary artery bypass grafting (CABG). Archives of Clinical Neuropsychology, 2007. 22(1): p. 73-85. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
308. Rosendahl, J., et al., Bypass surgery with psychological and spiritual support (the By.pass study): study design and research methods. American Heart Journal, 2009. 158(1): p. 8-14.e1. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
309. Rosengart, T.K., et al., Neurocognitive functioning in patients undergoing coronary artery bypass graft surgery or percutaneous coronary intervention: evidence of impairment before intervention compared with normal controls. Annals of Thoracic Surgery, 2005. 80(4): p. 1327-34; discussion 1334-5. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
310. Rothenhausler, H.-B., The effects of cardiac surgical procedures on health - related quality of life, cognitive performance, and emotional status outcomes: a prospective 6 - month follow - up study. Psychiatria Danubina, 2010. 22(1): p. 135-6. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
311. Rothenhausler, H.-B., et al., Psychiatric and psychosocial outcome of cardiac surgery with cardiopulmonary bypass: a prospective 12-month follow-up study. General Hospital Psychiatry, 2005. 27(1): p. 18-28. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
312. Royse, A.G., et al., Reduced neuropsychological dysfunction using epiaortic echocardiography and the exclusive Y graft. Annals of Thoracic Surgery, 2000. 69(5): p. 1431-8. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
313. Royse, C., et al., Prospective randomized trial of high thoracic epidural analgesia for coronary artery bypass surgery. Annals of Thoracic Surgery, 2003. 75(1): p. 93-100. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
314. Royse, C.F., et al., The influence of propofol or desflurane on postoperative cognitive dysfunction in patients undergoing coronary artery bypass surgery. Anaesthesia, 2011. 66(6): p. 455-64. POPULATION MEAN AGE <65
315. Rubens, F.D., et al., The cardiotomy trial: a randomized, double-blind study to assess the effect of processing of shed blood during cardiopulmonary bypass on transfusion and neurocognitive function. Circulation, 2007. 116(11 Suppl): p. I89-97. POPULATION MEAN AGE <65
316. Rudolph, J.L., et al., Independent Vascular and Cognitive Risk Factors for Postoperative Delirium. American Journal of Medicine, 2007. 120(9): p. 807-813. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
317. Rushford, N., et al., Recall of information received in hospital by female cardiac patients. European Journal of Cardiovascular Prevention & Rehabilitation, 2007. 14(3): p. 463-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
318. Saczynski, J.S., et al., Cognitive trajectories after postoperative delirium. New England Journal of Medicine, 2012. 367(1): p. 30-9. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
319. Sader, M.A., et al., Neuropsychological and psychiatric outcomes following coronary surgery or angioplasty: A comparative study. Heart Lung and Circulation, 2002. 11(2): p. 95-101. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
320. Sahu, B., et al., Neurocognitive function in patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass: the effect of two different rewarming strategies. Journal of Cardiothoracic & Vascular Anesthesia, 2009. 23(1): p. 14-21. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
321. Sakurai, M., et al., Cognitive dysfunction following cardiovascular surgery. Japanese Journal of Thoracic and Cardiovascular Surgery, 2005. 53(5): p. 251-254. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
322. Saleh, A.A., et al., Effect of temperature during cardiopulmonary bypass on neurocognitive function in open heart surgery. Egyptian Journal of Anaesthesia, 2005. 21(4): p. 317-321. FULL TEXT UNAVAILABLE
323. Salenius, J.P., et al., Late results of surgical and nonoperative treatment of carotid stenosis. Eighty-four patients documented by angiography in 1974-1976. Journal of Cardiovascular Surgery, 1990. 31(2): p. 156-61. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)

324. Samuels, M.A., Can cognition survive heart surgery? Circulation, 2006. 113(24): p. 2784-2786. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
325. Sandau, K.E., et al., Health-related quality of life and subjective neurocognitive function three months after coronary artery bypass graft surgery. Heart & Lung, 2008. 37(3): p. 161-72. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
326. Sasoh, M., et al., Effects of EC-IC bypass surgery on cognitive impairment in patients with hemodynamic cerebral ischemia. Surgical Neurology, 2003. 59(6): p. 455-460. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
327. Schmitz, C., et al., Off-Pump versus on-pump coronary artery bypass: can OPCAB reduce neurologic injury? Heart Surgery Forum, 2003. 6(3): p. 127-30. POPULATION MEAN AGE <65
328. Schmitz, C., et al., Can particulate extraction from the ascending aorta reduce neurologic injury in cardiac surgery? Journal of Thoracic and Cardiovascular Surgery, 2003. 126(6): p. 1829-1838. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
329. Schoen, J., et al., The association between gender, cognitive function, markers of inflammation and preoperative cerebral oxygen saturation in a cohort of preoperative cardiac surgery patients. Applied Cardiopulmonary Pathophysiology. 15(2): p. 62-70. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
330. Schoen, J., et al., Preoperative regional cerebral oxygen saturation is a predictor of postoperative delirium in on-pump cardiac surgery patients: A prospective observational trial. Critical Care. 15(5). NO POST-PROCEDURE MEASURE OF COGNITION
331. Scott, D.A., et al., Centrifugal versus roller head pumps for cardiopulmonary bypass: effect on early neuropsychologic outcomes after coronary artery surgery. Journal of Cardiothoracic & Vascular Anesthesia, 2002. 16(6): p. 715-22. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
332. Sebregts, E.H., et al. Psychological effects of a short behavior modification program in patients with acute myocardial infarction or coronary artery bypass grafting. A randomized controlled trial. Journal of psychosomatic research, 2005. 58, 417-24 DOI: 10.1016/j.jpsychores.2004.02.021. NO POST-PROCEDURE MEASURE OF COGNITION
333. Sellman, M., et al., A randomized study of neuropsychological function in patients undergoing coronary bypass surgery. Thoracic & Cardiovascular Surgeon, 1993. 41(6): p. 349-54. POPULATION MEAN AGE <65
334. Sellman, M., et al., Early neurological and electroencephalographic changes after coronary artery surgery in low-risk patients younger than 70 years. Thoracic & Cardiovascular Surgeon, 1991. 39(2): p. 76-80. NO POST-PROCEDURE MEASURE OF COGNITION
335. Selnes, O.A., Comparison of cerebral embolization during off-pump and on-pump coronary artery bypass surgery: Invited commentary. Annals of Thoracic Surgery, 2003. 76(3): p. 770. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
336. Selnes, O.A., et al., Cognition 6 years after surgical or medical therapy for coronary artery disease. Annals of Neurology, 2008. 63(5): p. 581-90. POPULATION MEAN AGE <65
337. Selnes, O.A., et al., Do management strategies for coronary artery disease influence 6-year cognitive outcomes? Annals of Thoracic Surgery, 2009. 88(2): p. 445-454. POPULATION MEAN AGE <65
338. Selnes, O.A., et al., Cognitive changes with coronary artery disease: a prospective study of coronary artery bypass graft patients and nonsurgical controls. Annals of Thoracic Surgery, 2003. 75(5): p. 1377-84; discussion 1384-6. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
339. Sendelbach, S., et al., Early neurocognitive function of patients after off-pump coronary artery bypass surgery. Heart & Lung, 2005. 34(6): p. 367-74. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
340. Sendelbach, S., et al., Correlates of neurocognitive function of patients after off-pump coronary artery bypass surgery. American Journal of Critical Care, 2006. 15(3): p. 290-8. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
341. Shaaban-Ali, M., et al., Changes in serum S100beta protein and Mini-Mental State Examination after cold (28 degrees C) and warm (34 degrees C) cardiopulmonary bypass using different blood gas strategies (alpha-stat and pH-stat). Acta Anaesthesiologica Scandinavica, 2002. 46(1): p. 10-6. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
342. Shelley, M., K.I. Pakenham, and I. Frazer Cortisol changes interact with the effects of a cognitive behavioural psychological preparation for surgery on 12-month outcomes for surgical heart patients. Psychology & health, 2009. 24, 1139-52 DOI: 10.1080/08870440802126704. POPULATION MEAN AGE <65
343. Shroyer, A.L., et al., On-pump versus off-pump coronary-artery bypass surgery. New England Journal of Medicine, 2009. 361(19): p. 1827-37. POPULATION MEAN AGE <65

344. Shuhaiber, J.H., et al., Randomized prospective trial for blood transfusion during adult cardiopulmonary bypass surgery [8] (multiple letters). Journal of Thoracic and Cardiovascular Surgery, 2005. 129(5): p. 1200-1202. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
345. Siepe, M., et al., Increased systemic perfusion pressure during cardiopulmonary bypass is associated with less early postoperative cognitive dysfunction and delirium. European Journal of Cardio-Thoracic Surgery, 2011. 40(1): p. 200-7. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
346. Silbert, B.S., et al., Preexisting cognitive impairment in patients scheduled for elective coronary artery bypass graft surgery. Anesthesia & Analgesia, 2007. 104(5): p. 1023-8, tables of contents. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
347. Sirkka, A., et al., Quality of life and cognitive performance after carotid endarterectomy during long-term follow-up. Acta Neurologica Scandinavica, 1992. 85(1): p. 58-62. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
348. Skrabal, C.A., et al., Effects of poly-2-methoxyethylacrylate (PMEA)-coating on CPB circuits. Scandinavian Cardiovascular Journal, 2006. 40(4): p. 224-9. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
349. Slater, J.P., et al., Cerebral oxygen desaturation predicts cognitive decline and longer hospital stay after cardiac surgery. Annals of Thoracic Surgery, 2009. 87(1): p. 36-44; discussion 44-5. POPULATION MEAN AGE <65
350. Sloan, F.A., et al., The effect of dementia on outcomes and process of care for Medicare beneficiaries admitted with acute myocardial infarction. Journal of the American Geriatrics Society, 2004. 52(2): p. 173-81. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
351. Smith, M.H., et al., Age and other risk factors for neuropsychologic decline in patients undergoing coronary artery bypass graft surgery. Journal of Cardiothoracic & Vascular Anesthesia, 2000. 14(4): p. 428-32. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
352. Smolderen, K.G., et al., The association of cognitive and somatic depressive symptoms with depression recognition and outcomes after myocardial infarction. Circulation: Cardiovascular Quality and Outcomes, 2009. 2(4): p. 328-337. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
353. Sousa Uva, M., et al., Early graft patency after off-pump and on-pump coronary bypass surgery: a prospective randomized study. European Heart Journal, 2010. 31(20): p. 2492-9. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
354. Spezzaferri, R., et al., Psychological disorders after coronary artery by-pass surgery: a one-year prospective study. Monaldi Archives for Chest Disease, 2009. 72(4): p. 200-5. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
355. Stables, R.H., Design of the 'Stent or Surgery' trial (SoS): a randomized controlled trial to compare coronary artery bypass grafting with percutaneous transluminal coronary angioplasty and primary stent implantation in patients with multi-vessel coronary artery disease. Seminars in Interventional Cardiology, 1999. 4(4): p. 201-7. NO POST-PROCEDURE MEASURE OF COGNITION
356. Stanley, T.O., et al., The impact of postoperative atrial fibrillation on neurocognitive outcome after coronary artery bypass graft surgery. Anesthesia & Analgesia, 2002. 94(2): p. 290-5, table of contents. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
357. Strauss, B., et al., Preoperative and late postoperative psychosocial state following coronary artery bypass surgery.[Erratum appears in Thorac Cardiovasc Surg 1992 Jun;40(3):167]. Thoracic & Cardiovascular Surgeon, 1992. 40(2): p. 59-64. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
358. Stroobant, N., et al., Short-term and long-term neurocognitive outcome in on-pump versus off-pump CABG. European Journal of Cardio-Thoracic Surgery, 2002. 22(4): p. 559-64. POPULATION MEAN AGE <65
359. Stroobant, N., et al., Neuropsychological functioning 3-5 years after coronary artery bypass grafting: does the pump make a difference? European Journal of Cardio-Thoracic Surgery, 2008. 34(2): p. 396-401. POPULATION MEAN AGE <65
360. Stroobant, N., et al., Relation between neurocognitive impairment, embolic load, and cerebrovascular reactivity following on- and off-pump coronary artery bypass grafting.[Erratum appears in Chest. 2006 Jan;129(1):216]. Chest, 2005. 127(6): p. 1967-76. POPULATION MEAN AGE <65
361. Stroobant, N. and G. Vingerhoets, Depression, anxiety, and neuropsychological performance in coronary artery bypass graft patients: a follow-up study. Psychosomatics, 2008. 49(4): p. 326-31. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
362. Stygall, J., et al. Cognitive change 5 years after coronary artery bypass surgery. Health psychology : official journal of the Division of Health Psychology, American Psychological Association, 2003. 22, 579-86 DOI: 10.1037/0278-6133.22.6.579. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST

363. Stygall, J., et al., Effect on the brain of two techniques of myocardial protection. Asian Cardiovascular & Thoracic Annals, 2009. 17(3): p. 259-65. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
364. Sugiyama, N., et al., The incidence and severity of cognitive decline after major noncardiac surgery: A comparison with that after cardiac surgery with cardiopulmonary bypass. Journal of Anesthesia, 2002. 16(3): p. 261-264. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
365. Suksompong, S., et al., Neuropsychological alterations after coronary artery bypass graft surgery. Journal of the Medical Association of Thailand, 2002. 85 Suppl 3: p. S910-6. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
366. Svenmarker, S., et al., Neurological and general outcome in low-risk coronary artery bypass patients using heparin coated circuits. European Journal of Cardio-Thoracic Surgery, 2001. 19(1): p. 47-53. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
367. Svenmarker, S., et al., Clinical effects of the heparin coated surface in cardiopulmonary bypass. European Journal of Cardio-Thoracic Surgery, 1997. 11(5): p. 957-64. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
368. Svensson, L.G., et al., A prospective randomized study of neurocognitive function and S-100 protein after antegrade or retrograde brain perfusion with hypothermic arrest for aortic surgery. Journal of Thoracic and Cardiovascular Surgery, 2000. 119(1): p. 163-166. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
369. Svensson, L.G., E.M. Nadolny, and W.A. Kimmel, Multimodal protocol influence on stroke and neurocognitive deficit prevention after ascending/arch aortic operations. Annals of Thoracic Surgery, 2002. 74(6): p. 2040-2046. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
370. Sweet, J.J., et al., Absence of cognitive decline one year after coronary bypass surgery: comparison to nonsurgical and healthy controls. Annals of Thoracic Surgery, 2008. 85(5): p. 1571-8. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
371. Taggart, D.P., et al. Serum S-100 protein concentration after cardiac surgery: a randomized trial of arterial line filtration. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, 1997. 11, 645-9. POPULATION MEAN AGE <65
372. Taggart, D.P., et al., Is cardiopulmonary bypass still the cause of cognitive dysfunction after cardiac operations? Journal of Thoracic & Cardiovascular Surgery, 1999. 118(3): p. 414-20; discussion 420-1. POPULATION MEAN AGE <65
373. Taggart, D.P., et al., Neuroprotection during cardiac surgery: a randomised trial of a platelet activating factor antagonist. Heart, 2003. 89(8): p. 897-900. NO POST-PROCEDURE MEASURE OF COGNITION
374. Takaiwa, A., et al., Changes in cognitive function during the 1-year period following endarterectomy and stenting of patients with high-grade carotid artery stenosis. Acta Neurochirurgica, 2009. 151(12): p. 1593-600. FULL TEXT UNAVAILABLE
375. Takaiwa, A., et al., Cognitive function in patients with severe carotid stenosis - Evaluation of RBANS, WAIS-R and NART before treatment of carotid revascularization. Brain and Nerve, 2006. 58(8): p. 681-686. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
376. Tardiff, B.E., et al., Preliminary report of a genetic basis for cognitive decline after cardiac operations. The Neurologic Outcome Research Group of the Duke Heart Center. Annals of Thoracic Surgery, 1997. 64(3): p. 715-20. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
377. Thalmann, M., et al., OPCAB: Reducing the Perioperative Risk Avoiding Extracorporeal Circulation in CABG Surgery. European Surgery - Acta Chirurgica Austriaca, 2003. 35(6): p. 327-329. NO POST-PROCEDURE MEASURE OF COGNITION
378. Thornton, E.W., et al., Quality of life outcomes after coronary artery bypass graft surgery: relationship to neuropsychologic deficit. Journal of Thoracic & Cardiovascular Surgery, 2005. 130(4): p. 1022-7. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
379. Toner, I., et al., Cerebral functional changes following cardiac surgery: Neuropsychological and EEG assessment. European Journal of Cardio-Thoracic Surgery, 1998. 13(1): p. 13-20. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
380. Tully, P.J., et al., Neuropsychologic and quality-of-life outcomes after coronary artery bypass surgery with and without cardiopulmonary bypass: a prospective randomized trial. Journal of Cardiothoracic & Vascular Anesthesia, 2008. 22(4): p. 515-21. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
381. Tully, P.J., et al., Neuropsychological function 5 years after cardiac surgery and the effect of psychological distress. Archives of Clinical Neuropsychology, 2009. 24:8 p. 741-51. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)

382. Turk, A.S., et al., Effect of carotid artery stenting on cognitive function in patients with carotid artery stenosis: preliminary results. Ajnr: American Journal of Neuroradiology, 2008. 29(2): p. 265-8. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
383. Uekermann, J., et al., Neuropsychological deficits after mechanical aortic valve replacement. Journal of Heart Valve Disease, 2005. 14(3): p. 338-43. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
384. Uva, M.S., et al. Rationale, design and methodology for a prospective randomized study of graft patency in off-pump and on-pump multi-vessel coronary artery bypass surgery (PROMISS) using multidetector computed tomography. Trials, 2008. 9, 44tn: isrctn58800729/isrctn. NO POST-PROCEDURE MEASURE OF COGNITION
385. Vaage, J., U. Jensen, and A. Ericsson, Neurologic injury in cardiac surgery: Aortic atherosclerosis emerges as the single most important risk factor. Scandinavian Cardiovascular Journal, 2000. 34(6): p. 550-557. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
386. van den Goor, J., et al., Improvement of cognitive test performance in patients undergoing primary CABG and other CPB-assisted cardiac procedures. Perfusion, 2008. 23(5): p. 267-73. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
387. van Dijk, D., et al., Beating heart versus conventional cardiopulmonary bypass: the octopus experience: a randomized comparison of 281 patients undergoing coronary artery bypass surgery with or without cardiopulmonary bypass. Seminars in Cardiothoracic & Vascular Anesthesia, 2006. 10(2): p. 167-70. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
388. Van Dijk, D., et al., Cognitive outcome after off-pump and on-pump coronary artery bypass graft surgery: a randomized trial. JAMA, 2002. 287(11): p. 1405-12. POPULATION MEAN AGE <65
389. van Dijk, D., et al., Association between early and three month cognitive outcome after off-pump and on-pump coronary bypass surgery. Heart, 2004. 90(4): p. 431-4. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
390. van Dijk, D., et al., Cognitive outcomes five years after not undergoing coronary artery bypass graft surgery. Annals of Thoracic Surgery, 2008. 85(1): p. 60-4. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
391. van Dijk, D., et al., Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. JAMA, 2007. 297(7): p. 701-8. NO POST-PROCEDURE MEASURE OF COGNITION
392. van Mastrigt, G.A.P.G., et al., Health-related quality of life after fast-track treatment results from a randomized controlled clinical equivalence trial. Quality of Life Research, 2010. 19(5): p. 631-42. POPULATION MEAN AGE <65
393. Vanninen, R., et al., Subclinical cerebral complications after coronary artery bypass grafting: prospective analysis with magnetic resonance imaging, quantitative electroencephalography, and neuropsychological assessment. Archives of Neurology, 1998. 55(5): p. 618-27. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
394. Venn, G.E., R.L. Patel, and D.J. Chambers, Cardiopulmonary bypass: perioperative cerebral blood flow and postoperative cognitive deficit. Annals of Thoracic Surgery, 1995. 59(5): p. 1331-5. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
395. Vingerhoets, G., et al., Prospective evaluation of verbal memory performance after cardiopulmonary bypass surgery. Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society, 1996. 18(2): p. 187-96. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
396. Vingerhoets, G., G. Van Nooten, and C. Jannes, Effect of asymptomatic carotid artery disease on cognitive outcome after cardiopulmonary bypass. Journal of the International Neuropsychological Society, 1996. 2(3): p. 236-9. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
397. Vingerhoets, G., G. Van Nooten, and C. Jannes, Neuropsychological impairment in candidates for cardiac surgery. Journal of the International Neuropsychological Society, 1997. 3(5): p. 480-484. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
398. Vingerhoets, G., et al., Short-term and long-term neuropsychological consequences of cardiac surgery with extracorporeal circulation. European Journal of Cardio-Thoracic Surgery, 1997. 11(3): p. 424-431. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
399. Von Waldegg, G.H. and A. Klement, Cognitive impairments after bypass surgery. Kognitive beeintrÃ¤chtigungen, 2009. 106(42): p. 693. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
400. Vuylsteke, A., et al., Circulatory arrest versus cerebral perfusion during pulmonary endarterectomy surgery (PEACOG): A randomised controlled trial. The Lancet. 378(9800): p. 1379-1387. POPULATION MEAN AGE <65
401. Wahlqvist, M., V. Denvall, and U. Havelius, No improvement of sustained attention after carotid endarterectomy as analysed by dark adaptometry. Cerebrovascular Diseases, 2003. 16(1): p. 91-4. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL

402. Wahrborg, P., et al., Neuropsychological outcome after percutaneous coronary intervention or coronary artery bypass grafting: results from the Stent or Surgery (SoS) Trial. Circulation, 2004. 110(22): p. 3411-7. POPULATION MEAN AGE <65
403. Wasser, K., et al., Age-dependent effects of carotid endarterectomy or stenting on cognitive performance. Journal of Neurology. 259(11): p. 2309-2318. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
404. Wasser, K., et al., New brain lesions after carotid revascularization are not associated with cognitive performance. Journal of Vascular Surgery, 2011. 53(1): p. 61-70. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
405. Weber, C.F., et al., Impact of general versus local anesthesia on early postoperative cognitive dysfunction following carotid endarterectomy: GALA Study Subgroup Analysis. World Journal of Surgery, 2009. 33(7): p. 1526-32. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
406. Weinstein, C.S., W.J. Woodard, and R.A. DeSilva, Late neurocognitive changes from neurological damage following coronary bypass surgery. Behavioral Medicine, 1998. 24(3): p. 131-7. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
407. Westaby, S., et al., Is there a relationship between cognitive dysfunction and systemic inflammatory response after cardiopulmonary bypass? Annals of Thoracic Surgery, 2001. 71(2): p. 667-72. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
408. Whitaker, D.C., J. Stygall, and S.P. Newman, Neuroprotection during cardiac surgery: Strategies to reduce cognitive decline. Perfusion, 2002. 17(SUPPL.): p. 69-75. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
409. Wilson, D.A., et al., Post-carotid endarterectomy neurocognitive decline is associated with cerebral blood flow asymmetry on post-operative magnetic resonance perfusion brain scans. Neurological Research, 2008. 30(3): p. 302-6. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
410. Witt, K., et al., Neuropsychological consequences of endarterectomy and endovascular angioplasty with stent placement for treatment of symptomatic carotid stenosis: a prospective randomised study. Journal of Neurology, 2007. 254(11): p. 1524-32. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
411. Xu, G., et al., Cognitive performance after carotid angioplasty and stenting with brain protection devices. Neurological Research, 2007. 29(3): p. 251-5. NO POST-PROCEDURE MEASURE OF COGNITION
412. Yamashita, T., et al., Combination of preoperative cerebral blood flow and 123I-iomazenil SPECT imaging predicts postoperative cognitive improvement in patients undergoing uncomplicated endarterectomy for unilateral carotid stenosis. Clinical Nuclear Medicine, 2012. 37(2): p. 128-33. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
413. Yates, S.L. and R.P. Alston, Neurological, psychological and cognitive sequelae of cardiac surgery. Current Anaesthesia and Critical Care, 2000. 11(4): p. 187-193. NOT RCT/CCT OR PROSPECTIVE OBS. TRIAL
414. Zamvar, V., et al., Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomised controlled trial. BMJ, 2002. 325(7375): p. 1268. NO COGNITIVE OUTCOMES AT LEAST 3 MONTHS POST-PROCEDURE
415. Zhang Z, Ma P, Xu Y, et al. Preventive effect of gastrodin on cognitive decline after cardiac surgery with cardiopulmonary bypass: a double-blind, randomized controlled study. J Huazhong Univ Sci Technolog Med Sci. 2011 Feb;31(1):120-7. PMID: 21336736. POPULATION MEAN AGE <65
416. Zimpfer, D., et al., Cognitive deficit after aortic valve replacement. Annals of Thoracic Surgery, 2002. 74(2): p. 407-12; discussion 412. PROSPECTIVE OBS. COHORT W/O CV PROCEDURE OF INTEREST
417. Zimpfer, D., et al., Long-term neurocognitive function after mechanical aortic valve replacement. Annals of Thoracic Surgery, 2006. 81(1): p. 29-33. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
418. Zimpfer, D., et al., Neurocognitive deficit following coronary artery bypass grafting: a prospective study of surgical patients and nonsurgical controls. Annals of Thoracic Surgery, 2004. 78(2): p. 513-8; discussion 518-9. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)
419. Zimpfer, D., et al., Neurocognitive deficit following aortic valve replacement with biological/mechanical prosthesis. European Journal of Cardio-Thoracic Surgery, 2003. 23(4): p. 544-51. SAMPLE SIZE <10 (RCT); <50 (PROSPECTIVE OBS. COHORT)

Appendix C

Search Strategy

Appendix C. Search Strategy

Database: Ovid MEDLINE(R) <1946 to January Week 3 2013>
Search Strategy:
---

1 comprehension/ (6633)
2 cognition disorders/ (44130)
3 auditory perceptual disorders/ (909)
4 memory/ (49313)
5 memory, episodic/ (472)
6 memory, long-term/ (371)
7 memory, short-term/ (13113)
8 mental recall/ (25327)
9 retention, psychology/ (7518)
10 memory disorders/ (13433)
11 exp Neuropsychological Tests/ (61191)
12 exp Executive Function/ (3065)
13 exp Psychometrics/ (49676)
14 exp Psychomotor Disorders/ (10067)
15 exp Psychomotor Performance/ (78939)
16 Dementia/ or Alzheimer disease/ or aphasia, primary progressive/ or dementia, vascular/ or frontotemporal lobar degeneration/ or lewy body disease/ (90697)
17 pick disease of the brain/ (351)
18 mild cognitive impairment/ (762)
19 central nervous system dysfunction.mp. (498)
20 neuropsychological impairment.mp. (860)
21 (Cognitive decline or cognitive dysfunction or cognitive tests or cognitive assessment or cognitive function or cognitive evaluation or cognitive performance or cognitive change or cognitive problem or cognitive outcome or cognitive sequelae).mp. (33149)
22 (Neuropsychologic* decline or neuropsychologic* dysfunction or neuropsychologic* tests or neuropsychologic* assessment or neuropsychologic* function or neuropsychologic* evaluation or neuropsychologic* performance or neuropsychologic* change or neuropsychologic* problem or neuropsychologic* outcome or neuropsychologic* sequelae).mp. (62490)
23 or/1-22 (364408)

24 Randomized controlled trials as topic/ (82496)
25 Randomized controlled trial/ (337448)
26 Random allocation/ (75972)
27 Double blind method/ (117175)
28 Single blind method/ (16885)
29 Clinical trial/ (472549)
30 Clinical trial, phase i.pt. (12507)
31 Clinical trial, phase ii.pt. (20105)
32 Clinical trial, phase iii.pt. (7375)
33 Clinical trial, phase iv.pt. (759)
34 Controlled clinical trial.pt. (84963)
35 Randomized controlled trial.pt. (337448)
36 Multicenter study.pt. (149119)
37 Clinical trial.pt. (472549)
38 exp clinical trials as topic/ (259816)
39 (clinical adj trial$).tw. (174974)
40 ((singl$ or doubl$ or treb$ or trip$) adj (blind$3 or mask$3)).tw. (114747)
41 Randomly allocated.tw. (14024)
42 (allocated adj2 random$).tw. (16356)
43 or/24-42 (1021274)

44 Epidemiologic studies/ (5512)
45 exp cohort studies/ (1215732)
46 (cohort adj (study or studies)).tw. (64056)
47 Cohort analy$.tw. (2848)
48 (follow up adj (study or studies)).tw. (33441)
49 (Observational adj (study or studies)).tw. (32538)

50 Longitudinal.tw. (112860)
51 or/44-50 (1316456)

52 Meta analysis/ (36638)
53 Meta analys$.tw. (41461)
54 literature review.mp. (35019)
55 (systematic adj (review or overview)).tw. (30248)
56 or/52-55 (106130)

57 43 or 51 or 56 (2182597)

58 Case report.tw. (170277)
59 letter/ (758034)
60 historical article/ (288506)
61 addresses/ (4019)
62 autobiography/ (2675)
63 Bibliography/ (14862)
64 Biography/ (156977)
65 Comment/ (484716)
66 Editorial/ (307072)
67 News/ (142112)
68 or/58-67 (1755076)

69 57 not 68 (2085235)

70 limit 69 to humans (1980119)
71 limit 70 to yr="1990 -Current" (1694926)
72 limit 71 to english language (1521263)
73 limit 72 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") (423582)
74 72 not 73 (1097681)

75 exp Myocardial Revascularization/ (75825)
76 exp percutaneous coronary intervention/ (32327)
77 Heart bypass, right/ (576)
78 Coronary revascularization.mp. (4172)
79 (coronary artery bypass graft or CABG).mp. (14519)
80 (percutaneous coronary intervention or PCI).mp. (15273)
81 coronary stent*.mp. (4595)
82 coronary angioplas*.mp. (11666)
83 or/75-82 (89913)

84 74 and 83 (28370)

85 exp Endarterectomy, Carotid/ (6306)
86 (carotid endarterectomy or CEA).mp. (20384)
87 (carotid artery stenting or CAS).mp. (54374)
88 carotid surg*.mp. (1111)
89 or/85-88 (76271)

90 74 and 89 (6030)

91 Heart valve prosthesis/ (26828)
92 exp Heart Valve Prosthesis Implantation/ (11217)
93 Cardiac valve annuloplasty/ (137)
94 (aortic valve replacement or AVR).mp. (8953)
95 (mitral valve replacement or MVR).mp. (5610)
96 (aortic valve repair or mitral valve repair).mp. (2378)
97 (aortic valve surg* or mitral valve surg*).mp. (2156)
98 or/91-97 (41284)

99 74 and 98 (5753)

100 exp Catheter Ablation/ (18600)
101 exp Ablation Techniques/ (82421)
102 100 or 101 (82421)

103 exp Atrial Fibrillation/ (30442)
104 atrial fibrillation ablation.mp. (446)
105 103 or 104 (30482)

106 102 and 105 (5004)

107 74 and 106 (1659)

108 23 and 84 (396)

109 23 and 90 (112)

110 23 and 99 (40)

111 23 and 107 (4)

112 or/108-111 (527)

Appendix D

Neuropsychological Test Descriptions

Most Commonly Reported Testing Procedures by Cognitive Domain

Total Studies Reviewed, N=21	*Count of Studies by Domain or Test*	
	N	***%***
Attention	**18**	**85.7**
Trail Making Test A *	16	76.2
Digit Span Forward	11	52.4
Language	**12**	**57.1**
Verbal Fluency Tests	10	47.6
Other Language Tests (includes BNT)	6	28.6
Boston Naming Test	4	19.1
Memory	**18**	**85.7**
Rey Auditory Verbal Learning Test *	9	42.9
Verbal List Learning Tests (includes RVLT)	15	71.4
Non-Verbal Memory Tests	5	23.8
Visuospatial	**7**	**33.3**
Spatial Span / Corsi Blocks	3	14.3
Other Visuospatial tests	4	19.1
Executive	**20**	**95.2**
Trail Making Test B *	18	85.7
Digit Symbol / Symbol Digit Modalities	11	52.4
Digit Span Backwards	10	47.6
Psychomotor	**14**	**66.7**
Grooved Pegboard *	10	47.6
Finger Tapping	4	19.1
Complex Reaction Time Tests	4	19.1
Intellectual Ability	**8**	**38.1**
FSIQ or IQ Estimate	5	23.8
National Adult Reading Tests	3	14.3
Screening Tests	**8**	**38.1**
Mini Mental State Exam	6	28.6
Montreal Cognitive Assessment	3	14.3

* Tests recommended by the 1995 Consensus Statement

Note. Although many testing procedures evaluate multiple cognitive abilities, for simplicity in reporting, all have been assigned to one primary domain. The reader is referred to Appendix J for detailed reporting of test results by cognitive domain in which tests are replicated across all relevant cognitive domains.

Brief Descriptions of the Most Commonly Used Measures/Testing Procedures

*The tests recommended by the 2005 consensus statement publication include the following:

Trail Making Test*

The Trail Making Test (TMT) is in the public domain and substantial normative data exists for clinical interpretation. In Trail A, subjects are asked to draw lines connecting circled numbers on a page in sequence as quickly as they can. In Trail B, one alternates between numbers and letters. In each condition, the primary score is the time to complete the task, and it is common to also track errors during performance. Trail A measures visual attention and processing speed. Trail B taps executive abilities including set shifting and mental flexibility. The TMT was included in the 2005 consensus statement recommendation, and was the most

commonly reported test in the studies reviewed (76% Trial A, 86% Trail B). Appropriately, most studies reported separate scores (time for completion) for Trail A and B or a difference score between the two conditions.

Digit Span

The Digit Span test is a subtest of both the Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Memory Scales (WMS). Subjects are read a sequence of numbers and asked to repeat the same sequence back to the examiner in order (forward span) or in reverse order (backward span). Forward span captures attention efficiency and capacity. Backward span is an executive task particularly dependent on working memory. The Digit Span subtest can be scored as one summary value (this is the score which is age-normed and contributes to summary scores in the Wechsler tests), or separately for forwards and backwards performance. Forwards and backwards performance can be reported either as subscores (the number of correct items of each type) or as span scores (the maximum number of digits correctly produced forwards or backwards by the subjects). Approximately half (forwards 52%, backwards 48%) of the studies reviewed reported Digit Span scores. There was relatively common use of the summary score, as opposed to reporting forward and backward span separately. Although this is how the subtest is totaled and age-normed for use in the Wechsler tests, it provides less information than evaluating separate forwards and backwards scores (age-based means and standard deviations are provided for individual forward and backward spans). When separate scores were provided for forwards and backwards, it was rarely stated whether these were Wechsler subscores scores (representing multiple items at each span level) or maximum span scores. Clear reporting not only of separate forwards and backwards scores, but also of the specific metric (subscore or maximal span) is essential to characterizing subject performance (demographic-based norming) and evaluating whether data can pooled across multiple studies.

Digit Symbol / Symbol Digit Modalities

Digit Symbol (from the Wechsler Adult Intelligence Scale) and Symbol Digit Modalities are similar symbol substitution tasks in which subjects are presented with rows of numbers (or symbols for Symbol Digit Modalities) and asked to substitute the corresponding symbol (or number) from a key provided above. The task is timed and subjects are asked to complete the task as quickly as possible. The primary score consists of the number of items completed in a specified amount of time (varies by version) and is influenced by psychomotor ability, sustained attention, processing speed and to a lesser degree working memory. Secondary metrics can be calculated to evaluate incidental learning during the testing procedure, and a copy/motor version of the task is available to evaluate the relative contribution of motor versus cognitive aspects of task performance. Approximately half of the studies reviewed report using either the Digit Symbol or Symbol Digit Modalities test (52%). Because there are multiple versions of this general test format, it is important to specify the specific version of the test used in order to characterizing subject performance (demographic-based norming) and evaluate whether data can pooled across multiple studies. In many cases, not enough information was reported in the publication to determine the exact version of the test administered (e.g. WAIS-R vs. WAIS-III).

Verbal Fluency Tests

Verbal fluency tests are measures of spontaneous verbal production. The two most common types are 1) phonemic fluency (letter fluency), in which one is asked to produce words beginning

with a specified letter or sound (often "F", "A" and "S" or "C", "F" and "L"), and 2) semantic fluency (category fluency), in which one is asked to produced words that belong to a specified category (often "animals" or "fruits and vegetables"). Subjects are asked to provide as many examples of the rule (letter or category) as they can in one minute. The primary score is the number responses produced minus errors (e.g., repeats or invalid responses such as proper nouns or out of letter/category). Phonemic fluency tests are most often scored summing the total words produced over three letters (one minute for each). Verbal fluency tests evaluate expressive language ability, executive function, and are influenced by processing speed and potentially memory (semantic). Verbal fluency tests were the most common language tests reported (48%), with phonemic (letter) fluency reported more frequently than semantic fluency. This may in part be due to phonemic fluency being the more difficult of the two tasks and having a somewhat stronger association with executive function. The studies reviewed varied in the specificity with which they reported verbal fluency testing procedures and it was often unclear whether phonemic or semantic testing was administered, and what specific letters or categories were used. Without this information, mean subject scores cannot be compared to relevant normative data to evaluate performance, and data across studies cannot be aggregated for analysis.

Boston Naming Test

The Boston Naming test is a test of confrontation naming in which subjects are asked to name objects presented visually as two dimensional line drawings in a booklet. If the subject fails to produce the correct name within 20 seconds, phonemic and/or semantic cues can be provided depending on whether the subject is able to correctly perceive the image. The primary score is the number of correctly identified objects within the initial 20 second presentation. Although the test evaluates language, not surprisingly, it is influenced by visuospatial deficits. The Boston Naming Test was the second most popular language test reported, used by 19% of studies. There are different forms of the test, primarily varying by the number of items presented. When reported, mean scores often appeared out of range for the most common 60-item version of the test, but no further specification was provided about the version administered. Again, this information is essential for evaluating performance and aggregating data across studies.

Tests of List Learning

Many studies reported verbal memory tests of list learning, in which subjects are read a list of words and asked to recall the list both immediately in learning trials and later for delayed recall trials, and often as a recognition task with the list embedded in distractor words. These tests evaluate verbal memory, both short and long term storage, as well as often the ability to benefit from learning strategies and cueing on recall (encoding versus storage). Seventy-one percent of the studies reviewed reported some type of verbal list learning task. The most commonly reported test of this type (43%) was the Rey Auditory Verbal Learning Test (RAVLT) which had been recommended in Murkin et al.'s 1995 consensus statement publication. There are often many different scores produced by these tests. Although most studies reported enough information to determine both the specific test (e.g. RAVLT, CVLT, CERAD) and score (e.g. sum of trials, free delayed recall, recognition hits), some failed to report this information. Additionally, there were cases in which a total summary score was calculated that is not commonly reported. Although this practice does not necessarily detract from the

individual study findings, it does make it more difficult to compare findings across studies and evaluate subject performance relevant to published normative data.

Grooved Pegboard

Many of the studies reviewed employed pegboard tests to evaluate their subjects' psychomotor ability. The most commonly reported (48%) was the Grooved Pegboard which had been recommended in Murkin et al.'s 1995 Consensus Statement publication. Grooved Pegboard tests manipulative dexterity, evaluating the coordination of fine motor movements on both sides of the body. Subjects are asked to place grooved pegs (like simple keys) into holes with matching slots such that the pegs must be rotated before they can be inserted. Multiple trials are administered separately for each the dominant and non-dominant hand, and the primary score is the time to complete 25 pegs. It is common to also record the number of times a subject drops a peg. The test requires visual and motor coordination, and is good for evaluating lateralized deficits such as those that may accompany stroke. Although Grooved Pegboard was very commonly reported, and most studies correctly presented dominant and non-dominant (or right vs. left) scores separately, many of the scores reported were substantially out of range of the published normative data for the study's reported subject demographics. Complete reporting of the specific testing procedures and scoring will help to make these results both more clinically meaningful and comparable across studies.

Appendix E

Patient Characteristics

Appendix E. Table 1. Summary of study baseline characteristics for all studies

Characteristic	Mean (range) *Unless otherwise note*	Number of trials reporting
Total number of patients evaluated	7802 (46 to 4752)	21
Total number of patients evaluated from RCTs, %	91 (n=7076; 46 to 4752)	17
Total number of patients evaluated from observational studies, %	9 (n=726; 64 to 326)	4
Study withdrawals (RCTs), % of patients	17 (5 to 41)	14
Age of subjects, years	68 (65 to 76)	21
Gender, male, % of patients	80 (41 to 93)	20
Race/ethnicity, white, % of patients	92 (92 to 93)	2
Education, high school, vocational school, or less, % of patients	60 (39 to 87)	4*
Education, post-secondary, % of patients	40 (13 to 61)	4*
Education, years	11 (7 to 14)	6
History of diabetes, % of patients	39 (0** to 47)	20
History of myocardial infarction, % of patients	36 (9 to 73)	13
History of stroke, % of patients	6 (0** to 8)	10†
History of depression, % of patients	0**	2
Studies conducted in United States/Canada, % of patients	17 (n=1350)	6
Studies conducted in Europe, % of patients	14 (n=1085)	11
Studies conducted in Australasia, % of patients	8 (n=615)	3
Multinational (North America and Europe), % of patients	61 (n=4752)	1
CABG studies, % of patients	93 (n=7265)	16
CEA/CAS studies, % of patients	5 (n=413)	3
AVR studies, % of patients	3 (n= 233)	3††

NR = not reported; RCT = randomized controlled trial; CAGB = Coronary artery bypass grafting; CEA = Carotid endarterectomy; CAS = Carotid artery stenting; AVR = Aortic valve replacement.
* In addition, one trial (Gold 1995) also reported that ≥90% of enrollees had at least a high school education.
** Indicates this was an exclusion criterion for study entry
† In addition, one CEA trial (Altinbas 2011) reported 46% of enrollees had a recent ischemic stroke based in imaging.
†† Percent and number of studies do not add up to 100% and 21, respectively. One study (Andrew 2001) has a CAGB arm as control.

Appendix E. Table 2. Summary of study baseline characteristics for CABG studies

Characteristic	Mean (range) *Unless otherwise note*	Number of trials reporting
Total number of patients evaluated	7265 (60 to 4752)	16
Total number of patients evaluated from RCTs, %	94 (n=6830; 60 to 4752)	14
Total number of patients evaluated from observational studies, %	6 (n=435; 109 to 326)	2
Study withdrawals (RCTs), % of patients	18 (5 to 41)	12
Age of subjects, years	68 (65 to 76)	16
Gender, male, % of patients	81 (60 to 93)	16
Race/ethnicity, white, % of patients	92 (92 to 93)	2
Education, high school, vocational school, or less, % of patients	60 (39 to 87)	4*
Education, post-high school, % of patients	40 (13 to 61)	4*
Education, years	12 (8 to 14)	5
History of diabetes, % of patients	40 (0* to 47)	15
History of myocardial infarction, % of patients	36 (9 to 73)	12
History of stroke, % of patients	6 (0** to 8)	10
History of depression, % of patients	0**	2
Studies conducted in United States/Canada, % of patients	19 (n=1350)	6
Studies conducted in Europe, % of patients	8 (n=548)	6
Studies conducted in Australasia, % of patients	8 (n=615)	3
Multinational (North America and Europe), % of patients	65 (n=4752)	1

NR = not reported; RCT = randomized controlled trial. CAGB = Coronary artery bypass grafting.
* In addition, one trial (Gold 1995) also reported that ≥90% of enrollees had at least a high school education.
** Indicates this was an exclusion criterion for study entry

Appendix E. Table 3. Summary of study baseline characteristics for AVR studies

Characteristic	Mean (range) *Unless otherwise note*	Number of trials reporting
Total number of patients evaluated	233 (60 to 109)	3
Total number of patients evaluated from RCTs	60	1
Total number of patients evaluated from observational studies	173 (64 to 109)	2
Study withdrawals (RCTs), % of patients	NR	-
Age of subjects, years	68 (66 to 74)	3
Gender, male, % of patients	66 (41 to 80)	2
Race/ethnicity, white, % of patients	NR	-
Education, high school, vocational school, or less, % of patients	NR	-
Education, post-high school, % of patients	NR	-
Education, years	10.2	1
History of diabetes, % of patients	22 (17 to 33)	3
History of myocardial infarction, % of patients	NR	-
History of stroke, % of patients	0*	1
History of depression, % of patients	NR	-
Studies conducted in United States/Canada, % of patients	0	
Studies conducted in Europe, % of patients	53 (n=124)	2
Studies conducted in Australasia, % of patients	47 (n=109)	1

NR = not reported; RCT = randomized controlled trial; AVR = Aortic valve replacement.
* Indicates this was an exclusion criterion for study entry

Appendix E. Table 4. Summary of study baseline characteristics for CAS / CEA studies

Characteristic	Mean (range) *Unless otherwise note*	Number of trials reporting
Total number of patients evaluated	413 (46 to 227)	3
Total number of patients evaluated from RCTs	186 (46 to 140)	2
Total number of patients evaluated from observational studies	227	1
Study withdrawals (RCTs), % of patients	15 (13 to 15)	2
Age of subjects, years	72 (68 to 74)	3
Gender, male, % of patients	72 (71 to 74)	3
Race/ethnicity, white, % of patients	NR	-
Education, high school, vocational school, or less, % of patients	NR	-
Education, post-high school, % of patients	NR	-
Education, years	7.2	1*
History of diabetes, % of patients	28 (7 to 36)	3
History of myocardial infarction, % of patients	16	1
History of stroke, % of patients	46**	1
History of depression, % of patients	NR	-
Studies conducted in United States/Canada, % of patients	0	
Studies conducted in Europe, % of patients	100 (n=413)	3
Studies conducted in Australasia, % of patients	0	

NR = not reported; RCT = randomized controlled trial; CEA = Carotid endarterectomy; CAS = Carotid artery stenting; AVR = Aortic valve replacement.
* Another study (Altinbas) also reported education with undefined units.
** Recent ischemic stroke based in imaging.

Appendix F

Risk of Bias

Appendix F. Table 1. Assessment of individual study quality for Randomized controlled trials/Controlled clinical trials based on risk of bias (low-risk, high-risk, or unclear)

Study year	Random sequence generation	Allocation concealment	Masking	Attrition bias accounted for	Intention-to-treat analysis	Selective outcomes reporting	Overall risk of bias*
CABG Studies							
Lamy, 2013[1]	Low-risk	Low-risk	Low-risk	Low-risk	High-risk	Low-risk	Moderate
Jensen, 2008[2]	Low-risk	Low-risk	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
Vedin, 2006[3]	Unclear	Unclear	Unclear	Low-risk	High-risk**	Low-risk	Unclear
Lund, 2005[4]	Unclear	Unclear	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
Lee, 2003[5]	Unclear	Unclear	Low-risk	Low-risk	High-risk**	Low-risk	Unclear
Boodhwani, 2007[6]	Low-risk	Low-risk	Low-risk	Unclear	High-risk**	Low-risk	Moderate
Nathan, 2001[7]**/2007**[8]	Low-risk	Low-risk	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
Djaiani, 2012[9]	Low-risk	Unclear	Low-risk	Unclear	High-risk*	Low-risk	Unclear
Anastasiadis, 2011[10]	Low-risk	Low-risk	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
Flesch, 2009[11]	Unclear	Unclear	Unclear	Low-risk	High-risk**	Low-risk	Unclear
Silbert, 2006[12]	Low-risk	Unclear	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
Alex, 2005[13]	Low-risk	Low-risk	Low-risk	Unclear	Unclear	Low-risk	Unclear
Kadoi, 2003[14]	Unclear	Unclear	Low-risk	Unclear	High-risk**	Low-risk	Unclear
Gold, 1995[15]	Low-risk	Unclear	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
CAS/CEA Studies							
Altinbas, 2011[16]	Low-risk	Low-risk	Unclear	Low-risk	High-risk**	Low-risk	Moderate
Crawley, 2000[17]	Low-risk	Low-risk	Low-risk	Low-risk	High-risk**	Low-risk	Moderate
AVR Studies							
Fakin, 2012[18]	Low-risk	Unclear	Unclear	Unclear	Unclear	Low-risk	Unclear

CABG = Coronary artery bypass grafting; CAS = carotid artery stenting; CEA = Carotid endarectomy; AVR=aortic valve replacement

Appendix F. Table 1. Assessment of individual study quality for Randomized controlled trials/Controlled clinical trials based on risk of bias (low-risk, high-risk, or unclear)

* Low risk of bias when individual interventional studies meet all quality criteria, a moderate risk of bias if at least one of the quality criteria is not met, high risk of bias if multiple quality criteria are not met, and unclear risk of bias if sequence generation, allocation concealment, and blinding methods were not reported. ** Completers only

Appendix F. Table 2. Assessment of individual study quality for observational studies based on risk of bias (low-risk, high-risk, or unclear)

Study year	Baseline groups similar in prognostic indicators	Attrition bias accounted for	Masking	Reporting bias from selective outcomes reporting	Overall risk of bias*
McKhann, 2009[19]/ Selnes, 2009[20]	High-risk	High-risk	Unclear	Low-risk	High
Andrew, 2001[21]	Low-risk	Low-risk	Unclear	Low-risk	Moderate
Baracchini, 2012[22]	High-risk	High-risk	Low-risk	Low-risk	High
Knipp, 2013[23]	High-risk	High-risk	Unclear	Low-risk	High

* Low risk of bias when individual prospective observational cohort studies meet all quality criteria, a moderate risk of bias if at least one of the quality criteria is not met, and a high risk of bias if multiple quality criteria are not met

Appendix G

Evidence Tables

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	**Inclusion/Exclusion Criteria**	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
Lamy, 2013[1] **The CABG Off or On Pump Revascular-ization Study (CORONARY)** Location: Multinational (19 countries) Funding Source: Government Study design: RCT	Inclusion Criteria: patients who required isolated CABG with median sternotomy and had one or more of the following risk factors: age of ≥70 years; the presence of peripheral arterial disease, cerebrovascular disease or carotid stenosis ≥70%; or renal insufficiency. Patients 60 to 69 years of age were eligible if they had at least one of the following risk factors: presence of diabetes (requiring an oral hypoglycemic agent, insulin, or both), urgent revascular-ization (after an acute coronary syndrome), left ventricular ejection fraction of ≤35%, or a recent history of smoking (<1 year before randomization). Exclusion Criteria: planned valve surgery, any contra-indication to off-pump CABG or on-pump CABG, a decision by a surgeon that one of the two techniques was not feasible for that patient, a life expectancy of <2 years, emergency or repeat CABG surgery.	N=4752 [Age (yr): 68 Gender (Male %): 81 Race/Ethnicity (%): NR Education (%): NR Weight: BMI: 27 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 47 History of HTN (%): 76 History of CAD (%):100 (presumed) History of CHF (%): 6 History of MI (%): 34 History of Stroke (%): 7 History of TIA (%): NR History of PAD (%): 8 Current smoker (%): NR, never smoked 46% Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CABG performed off-pump (n=2375; 721 and 989 completed Trails Making B and Digit Symbol Substitution Test, respectively) Control: CABG performed on-pump (n=2377; 711 and 986 completed Trails Making B and Digit Symbol Substitution Test, respectively)) **Procedure characteristics** Anesthesia type/duration: NR Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 3 months,12 months Study withdrawals, % (n/N): 9 (421/4752) did not undergo their assigned treatment (21%; 87/421) or converted to the other treatment (79%; 334/421) within 30 days of randomization	Random sequence generation: low Allocation Concealment: low, 24-hour automated voice-activated telephone randomization service Masking outcomes assessment: low, Primary outcomes reviewd by an adjudication committee whose members were unaware of study-group assignments. Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: neurocognitive assessments were originally intended to be mandatory for all participants but were made optional early in the course of the trial to improve recruitment. The decision about a patient's participation in these assessments was made on an individual basis; centers could select for these assessments patients who might be more likely to return to the hospital during the follow-up period to complete the tests. The decision to participate was made before randomization, to avoid biases. Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
Jensen, 2006;[24] 2008[2] Location: Denmark Funding Source: Non-industry (Danish Heart Foundation, Copenhagen Hospital Corporation's Research Council, Lundbeck Foundation) Study design: (RCT, follow-up to Jensen 2006). The study is a substudy of the Best Bypass Surgery (BBS) randomized trial	Inclusion Criteria: known ischemic 3-vessel heart disease affecting 1 of the marginal coronary arteries; scheduled for elective or subacute CABG at, Copenhagen University Hospital; 55 yrs of age or older; EuroSCORE (European system for cardiac operative risk evaluation) ≥5 Exclusion Criteria: previous heart surgery; ejection fraction < 30%; unstable pre-procedure condition; unable to give informed consent; MMSE score < 24; current severe psychiatric disease (depression, psychosis, or alcoholism [patients currently using antipsychotic or anti-depressant drugs or imbibing more than 5 drinks/units of alcohol per day within the last 3 months]); neuro-psychological testing within the last year; severe visual or auditory disorder.	N=120 Age (yr): 76 Gender (Male %): 60 Race/Ethnicity (%): NR Education (%): high school: 39 vocational: 53 university: 8 Weight: NR BMI: 27 Systolic BP (mm Hg): 146 Diastolic BP (mm Hg): 74 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 18 History of HTN (%): 61 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 73 History of Stroke (%): NR History of TIA (%): NR Previous neurological conditions, including stroke or TIA (%): 23 History of PAD (%): NR Current smoker (%): 18 Alcohol intake: NR (≤ 5/day to be included) Depression (%): 0 (excluded) Anxiety (%): NR	CV procedure: CABG performed on the beating heart with stabilization of the target coronary arteries (off-pump) (n=61 randomized, 47 included in 12 month follow-up) Control: CABG using cardio-pulmonary bypass with normothermia, aortic cross-clamping, and cold blood cardioplegic arrest (on-pump); patients with pronounced aortic calcifications were converted to off-pump surgery, according to BBS trial protocol (n=59 randomized, 43 included in 12 month follow-up) **Procedure characteristics** Anesthesia type/duration: NR Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 3 months,12 months Study withdrawals, % (n/N): 12.5 (15/120) at 3 months, 25 (30/120) at 12 months	Random sequence generation: low, centrally randomized by an external touchtone telephone voice-response system Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors and data analysts were blinded to treatment group Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: high, completers-only analysis Reporting bias from selective outcomes reporting: unclear, results of individual neurocognitive tests are not reported, but all prespecified results for neurocognitive dysfunction are reported
Vedin, 2006[3] Location: Sweden Funding Source: Non-industry and industry	Inclusion Criteria: admitted for elective CABG Exclusion Criteria: age under 50 or over 80 yrs, ejection fraction <30%, serum creatinine >150 µmol/L, tight (>70%) main	N=74 (4 patients either withdrew from the study before surgery or were excluded due to change of surgeons) Age (yr): 65 Gender (Male %): 80 Race/Ethnicity (%): NR Education (%): Completed university: 13	CV procedure: CABG performed off-pump (n=33) Control: CABG performed on-pump (n=37) **Procedure characteristics** Anesthesia type/duration:	Random sequence generation: unclear, randomization method NR Allocation Concealment: unclear, NR Masking outcomes assessment: unclear, NR

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	Risk of bias assessment (Low, moderate, high, unclear)
(Swedish Heart and Lung Foundation, The Swedish Research Council, The Vårdal Foundation, Karolinska Institutet, Karolinska University Hospital, and TERUMO EUROPE N.V Study design: RCT	stem stenosis, redo operation, diffuse distal coronary artery disease, unstable angina	Completed high school: 40 Completed junior high: 47 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 70 History of DM (%): 19 History of HTN (%): 49 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 34 History of Stroke (%): NR History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Current or former smoker (%): 63 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	anesthesia induced with fentanyl, midazolam and propofol and muscular relaxation achieved with pancuronium or atracurium/ bypass time 67 min (on-pump only); operative time 173 min Adjunctive neuroprotective treatments: 500 mg acetylsalicylic acid rectally on the evening of the operation and then 160 mg orally from the first post-operative day Cognitive assessment follow-up time points: 1 week, 1 month, 6 months Study withdrawals (%): 5 (4/74) at 6 months	Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported by group Intention to Treat Analysis: unclear, ITT analysis with regard to crossovers, but completers-only analysis with regard to those lost to follow-up Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Lund, 2005[4] Location: Norway Funding Source: Non-industry (Norwegian Council on Cardiovascuclar Diseases) Study design: RCT	Inclusion Criteria: between 40 and 80 yrs of age with stable angina pectoris and moderate or good left ventricular function Exclusion Criteria: ejection fraction of < 0.30 or renal failure (serum creatinine concentration >200 mmol/L [sic; probably should be µmol/L])	N=120 Age (yr): 65 Gender (Male %): 78 Race/Ethnicity (%): NR Education (yrs): 10.4 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): NR History of HTN (%): 43 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 45 History of Stroke or TIA (%): 8	CV procedure: CABG performed off-pump without cooling, cardiopulmonary bypass, or aortic cannulation (n=60) Control: CABG performed on-pump with moderate general hypothermia (28° to 32°C) using topical ice slush (n=60) **Procedure characteristics** Anesthesia type/duration: balanced anesthesia using opiates and barbiturates together with inhalation anesthesia. Propofol was given at the end of the	Random sequence generation: unclear, randomization method NR Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors (neuro-psychologist and neuroradiologist) were blinded to treatment group Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported by group Intention to Treat Analysis: no, completers-only analysis

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
		History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	operation to allow early extubation/bypass time NR, operative time 176.6 min (off pump 192 min vs. on-pump 162 [p=0.001] Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 3 months, 12 months Study withdrawals, % (n/N): 12 (14/120) at 3 months and 12 months	Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Lee, 2003[5] Location: US Funding Source: Non-industry (Hawaii Community Foundation Black Fund) Study design: RCT	Inclusion Criteria: undergoing first-time elective operation; no significant renal dysfunction (creatinine ≤2.0 mg/dL); able to undergo either procedure safely in the opinion of the surgeon Exclusion Criteria: NR	N=60 Age (yr): 66 Gender (Male %): 77 Race/Ethnicity (%): NR Education: 12 yrs Weight: 168 lbs BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 50 History of DM (%): 29 History of HTN (%): 79 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 9 History of Stroke (%): 5 History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CABG performed off-pump (n=30) Control: CABG performed on-pump using standard technique (n=30) **Procedure characteristics** Anesthesia type/duration: Anesthesia was provided in a consistent manner for both CABG and OPCAB patients/ bypass time NR; operative time: 4.1 hours Adjunctive neuroprotective treatments: Aspirin or Plavix ≤7 days prior to procedure Cognitive assessment follow-up time points: 0.5 months, 12 months Study withdrawals, % (n/N): 12	Random sequence generation: unclear, randomization method NR Allocation Concealment: unclear, sealed envelopes Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported by group Intention to Treat Analysis: no, completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
			(7/60) at 12 months	
McKhann, 2009;[19] Selnes, 2007;[25] Selnes, 2005[26] Location: US Funding Source: Non-industry (National Institute of Neurological Diseases and Stroke, Johns Hopkins Medical Institutions GCRC, Dana Foundation) Study design: Prospective observational cohort study	Inclusion Criteria: native English speakers, not mechanically ventilated, able to sit upright, able to give informed consent Exclusion Criteria: NR	**From Selnes 2007:** N=326 *Percents for groups reported for the variables considered unbalanced; Off-CABG=OffC; On-CABG=OnC; Nonsurgical cardiac controls=NSC* Age (yr): 65 Gender (Male %): 75 Race/Ethnicity (%):92 Caucasian Education (yrs): 14 Weight: NR BMI: NR Systolic BP (mm Hg): 134 Diastolic BP (mm Hg): 75 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 29 *(OffC 37 vs. OnC 30 vs. NSC 22)* History of HTN (%): 61 *(OffC 68 vs. OnC 64 vs. NSC 52)* History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 50 History of Stroke (%): 4 History of TIA (%): 4 History of PAD (%): 15 *(OffC 25 vs. OnC 16 vs. NSC 6)* Current smoker (%):10 *(OffC 16 vs. OnC 11 vs. NSC 4)* Alcohol intake: NR Depression (%): NR Anxiety (%): NR	**From Selnes 2007:** CV procedure: CABG performed off-pump (n=75). Control: CABG performed on-pump (n=152) Control: Patients diagnosed with coronary artery disease by cardiac catheterization under medical management (nonsurgical cardiac controls) (n=99) Procedure characteristics Anesthesia type/duration: All CABG patients were intubated and received general anesthesia using low-to-intermediate dose narcotics, inhalation agents, and paralytics. Bypass time NR; length of general anesthesia 284 min (off-pump 271 min vs. on-pump 291 min [p=0.03]) Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 3, 12, 36, and 72 months Study withdrawals, ie, did not complete cognitive testing, % (n/N): • **From McKhann 2009**: 58/312 (18.6) at 3 months, 54/312 (17.3) at 1 year,	Baseline groups similar in important prognostic indicators: high, groups had important differences in medical histories Attrition bias accounted for: high, numbers and reasons for loss to follow-up are described, but differ between groups Masking outcomes assessment: unclear, NR Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
			150/312 (48.1) at 3 years, 115/312 (36.9) at 6 years • **From Selnes 2007**: 60/326 (18.4) at 3 months, 56/326 (17.2) at 1 year, 152/326 (46.6) at 3 years	
Boodhwani, 2007[6] Location: Canada Funding Source: Non-industry (Canadian Institutes for Health Research) Study design: RCT Note: some details from another report from same trial, PMID 15115982	Inclusion Criteria: age 60 yrs or older; scheduled for non-urgent coronary artery surgery Exclusion Criteria: known neurologic deficits (previous stroke, history of Parkinson disease, Canadian Neurological Scale score <11.5, or abnormal Modified MMSE scores), serum creatinine greater than twice the normal level, or undergoing repeat cardiac surgery	N=267 Age (yr): 69 Gender (Male %): 88 Race/Ethnicity (%): NR Education (%): Less than Grade 9: 13 Grades 9-12: 45 Postsecondary: 43 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 35 History of HTN (%): NR History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): NR History of Stroke (%): 0 (excluded) History of TIA (%): NR History of PAD (%): 15 Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CABG with intraoperative nasopharyngeal temperature of 34°C (hypothermic) (n=133) Control: CABG with intraoperative nasopharyngeal temperature 37°C (normothermic) (n=134) **<u>Procedure characteristics</u>** Anesthesia type/duration: Anesthesia was induced with midazolam and sufentanil and maintained with isoflurane, as well as with sufentanil and midazolam or propofol infusions/ bypass time 75 min Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: pre-discharge, 3 months Study withdrawals, % (n/N): 12 (31/267) at 3 months	Random sequence generation: low, computer-generated randomization list Allocation Concealment: low, treatment assignment was concealed in opaque, sealed envelopes Masking outcomes assessment: low, participants and outcome assessors were unaware of treatment assignment, care providers were aware of treatment assignment Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported Intention to Treat Analysis: high completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Nathan, 2001;[7] **2007**[8] Location: Canada Funding Source:	Inclusion Criteria: age older than 60 yrs, accepted for CABG Exclusion Criteria: history of neurological deficits, non-	N=223 [131 at 5 yrs] Age (yr): 68 Gender (Male %): 85 Race/Ethnicity (%): NR Education: (%) Grade 8 or less: 33	CV procedure: CABG with rewarming to 34°C (hpothermic) (n=111) Control: CABG with rewarming to 37°C	Random sequence generation: low, computer-generated randomization Allocation Concealment: low, sealed opaque envelope

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	Risk of bias assessment (Low, moderate, high, unclear)
Non-industry (Heart and Stroke Foundation of Ontario) Study design: RCT	English-speaking, impediment to completing neuropsychological testing	Grade 9-12: 32 College/university: 35 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 24 History of HTN (%): NR History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	(normothermic) (n=112) Procedure characteristics Anesthesia type/duration: general anesthesia with cardiopulmonary bypass /bypass time 85 min Adjunctive neuroprotective treatments: arterial line filter Cognitive assessment follow-up time points: 3 months, 5 yrs Study withdrawals, % (n/N): 29 (64/223) at 3 months; 41 (92/223) at 5 yrs	Masking outcomes assessment: low, those assessing outcomes and the patient were unaware of the treatment group Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: no, 5-year results used a completers-only analysis (7 day and 3-month analysis was ITT using last-observation-carried-forward for missing data) Reporting bias from selective outcomes reporting: moderate, no neurocognitive outcomes reported for 3 months interval, all prespecified outcomes were reported for 5-yr interval
Djaiani, 2012[9] Location: Canada Funding Source: Non-industry (Heart and Stroke Foundation of Ontario) Study design: RCT Note: some	Inclusion Criteria: older than 60 yrs, scheduled for elective CABG surgery. Exclusion Criteria: surgical procedure in addition to CABG; redo CABG surgery; emergent surgery; severe kidney or liver disease (creatinine>133 [sic; probably should be 1.33] mg/ dL or bilirubin>2 mg/ dL); symptomatic cerebro-vascular disease; history of stroke, transient ischemic	N=226 randomized, 170 completed 12-month follow-up (only completers reported) Age (yr): 67 Gender (Male %): 90 Race/Ethnicity (%): NR Education: NR Weight: 83.2 kg BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 40	CV procedure: CABG with cell saver (n=84) Control: CABG with cardiotomy suction (n=86) **<u>Procedure characteristics</u>** Anesthesia type/duration: Anesthetic technique was standardized to include fentanyl, midazolam, pancuronium, and isoflurane. All patients received tranexamic acid 50 mg/kg intravenously after induction of	Random sequence generation: low, computer-generated randomization code Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
details from another report from same trial, PMID 17923575	attack, or atrial fibrillation; unable to complete the preoperative assessment; not able to speak English	History of HTN (%): 78 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 39 History of Stroke (%): 0 (excluded) History of TIA (%): 0 (excluded) History of PAD (%): 6 Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	anesthesia /bypass time 91 min Adjunctive neuroprotective treatments: arterial line filter Cognitive assessment follow-up time points: 6 weeks, 12 months. Study withdrawals, % (n/N): 25 (56/226) at 12 months	Intention to Treat Analysis: no, completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Anastasiadis, 2011[10] Location: Greece Funding Source: NR Study design: RCT	Inclusion Criteria: undergoing elective CABG surgery Exclusion Criteria: previous psychiatric illness (e.g. depression, schizophrenia), inability to undergo a proper neuropsychological assessment (due to language difficulties or poor educational status), history of stroke or >60% carotid artery stenosis as assessed by duplex ultrasonography pre-procedurally	N=64 Age (yr): 65 Gender (Male %): 93 Race/Ethnicity (%): NR Education, yrs: 7.9 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 23 History of HTN (%): 57 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%),within 30 days: 15 History of Stroke (%): NR History of TIA (%): NR History of PAD (%): 17 Current smoker (%): NR Alcohol intake: NR Depression (%): 0 (excluded) Anxiety (%): NR	CV procedure: CABG with minimal extracorporeal circulation (MECC), a closed CPB circuit containing a RotaFlow centrifugal pump and a Quadrox D diffusion membrane oxygenator (n=32) Control: CABG with conventional extracorporeal circulation (CECC), a standard open CPB circuit (n=32) **Procedure characteristics** Anesthesia type/duration: All patients received a standardized anesthetic protocol. General anesthesia was induced with 1-3 mg midazolam, 5-10 mg/kg fentanyl and 2-3 mg/kg propofol/bypass time 119.6 min Adjunctive neuroprotective treatments: NR Cognitive assessment follow-	Random sequence generation: low, computer generated random allocation Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: no, completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
			up time point: 3 months Study withdrawals, % (n/N): 6 (4/64) at 3 months	
Flesch, 2009[11] Location: Germany Funding Source: Industry (Takeda Pharma GmbH, Aachen, Germany) Study design: RCT	Inclusion Criteria: undergoing elective CABG; age 65 to 85 yrs; essential arterial hypertension Exclusion Criteria: neurological disorder or dementia (<8 points in the DemTect dementia screening test at baseline); creatinine level >2.0 mg/dL; acute myocardial infarction, stroke, or transient ischemic attack in the previous 3 months; required chronic treatment with an angiotensin-converting-enzyme inhibitor and/or angiotensin1 receptor antagonist; objection to study participation by admitting cardiologist; serum potassium level outside normal range; hemo-dynamically relevant stenosis of the aortic valve; relevant stenosis of the carotid artery; systolic blood pressure <110 mm Hg or episodes of hypotension; severe or uncontrolled hypertension (systolic BP ≥ 200 mmHg or diastolic BP ≥ 105 mmHg); known hyper-sensitivity to angiotensin1 receptor antagonists;	N=106 randomized, 87 completed 8-day follow-up (only completers reported) Age (yr): 71 Gender (Male %): 80 Race/Ethnicity (%): NR Education: NR Weight: NR BMI (mean ± SD): 27.4 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 83 History of DM (%): 35 History of HTN (%): 100 Untreated hypertension: 2.3 Previous antihypertensive therapy: 98 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 32 History of Stroke (%): 1 History of TIA (%): NR History of PAD (%): NR Current smoker (%): 6 Alcohol intake: NR Depression (%): NR	CV procedure: CABG with candesartan 8 mg/day for 6-11 days prior to surgery (n=53 randomized, 43 completed 8-day follow-up) Control: CABG with placebo for 6-11 days prior to surgery (n=53 randomized, 44 completed 8-day follow-up) **Procedure characteristics** Anesthesia type/duration: ethmidate, sufentanyl and rocuronium IV for induction, isoflurane for maintenance; bypass time, 86.2 min Adjunctive neuroprotective treatments: arterial line filter Cognitive assessment follow-up time points: 8 days, approximately 90 days Study withdrawals, % (n/N): 18 (19/106) at 90 days	Random sequence generation: Unclear: NR Allocation Concealment: Unclear: NR Masking outcomes assessment: unclear, NR Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: no, trial describes itself as intent-to-treat analysis, but it is actually a completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
	interventional treatment for renal artery stenosis within the last year; any relevant liver diseases; history of cancer in the last 5 yrs; life threatening diseases; any drug addiction and/or extensive use of alcohol; previous psychiatric illness; participation in another clinical investigation within 30 days prior to study enrollment			
Silbert, 2006[12] Location: Australia Funding Source: Non-industry (National Health and Medical Research Council, Canberra, Australian Capital Territory, Australia; National [Australian] Health and Medical Research Council) Study design: RCT	Inclusion Criteria: age 55 yrs or older, scheduled to undergo elective first-time CABG surgery, no previous neurologic deficit, and able to undergo neuropsychological testing Exclusion Criteria: not suitable for low-dose anesthesia and early extubation (e.g., ejection fraction < 30%, major systemic illness contraindicating early extubation); anticipated difficult neuropsychological assessment (e.g., English not the prime language, psychiatric illness)	N=350 randomized, 326 analyzed Age (yr): 68 Gender (Male %): 77 Race/Ethnicity (%): NR Education: NR Weight (kg): 82.2 BMI: 28.3 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 76 History of DM (%): 27 History of HTN (%): 71 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 47 History of Stroke (%): NR History of TIA (%): NR History of PAD (%): 12 Current smoker (%): NR History of smoking (%): 74 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CABG performed on-pump with low dose fentanyl 10 mcg/kg for induction; 2 mcg/kg boluses for maintenance as needed (n=180randomized and 168 retained, 161 completed 3 month tests, 159 completed 6 month tests) Control: CABG performed on-pump with high dose fentanyl 50 mcg/kg for induction (n=170 randomized and 158 retained, 142 completed 3 month tests, 141 completed 6 months tests) **Procedure characteristics** Anesthesia type/duration: rocuronium or vecuronium for induction with propofol for maintenance/ bypass time 100.8 min Adjunctive neuroprotective treatments: arterial line filter	Random sequence generation: low, random number tables stratified by institution and by on-pump vs. off-pump Allocation Concealment: unclear, "randomization was not revealed to the anesthesiologist until after the placement of invasive monitoring lines" Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: no, completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
			Cognitive assessment follow-up time points: 1 week, 3 months, 12 months Study withdrawals, % (n/N): 13.4 (47/350) at 3 months, 14.3 (50/350) at 12 months	
Alex, 2005[13] Location: United Kingdom Funding Source: NR Study design: RCT	Inclusion Criteria: patients scheduled to undergo on-pump coronary revascularization Exclusion Criteria: emergency operation, age older than 80 yrs, previous cerebrovascular disease, poor English language skills, learning difficulty, visual or hearing impairment, claustrophobia, history of pneumothorax, middle ear disease, and immunosuppressive or steroid therapy	N= 64 Age (yr): 66 Gender (Male %): 86 Race/Ethnicity (%): NR Education: NR Weight: NR BMI: 27.0 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 14 History of HTN (%): 65 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): 21 History of Stroke (%): NR History of TIA (%): 0 (excluded) History of PAD (%): 6.2 Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CABG with hyperbaric oxygen, 2.4 atmospheres absolute at 24, 12, and 4 hours before CABG (n=33) Control description: CABG with atmospheric air 1.5 atmospheres absolute at 24, 12, and 4 hours before CABG (n=31) **Procedure characteristics** Anesthesia type/duration: Anesthetic, bypass, and operative techniques were standardized in all patients/ bypass time 51 min Adjunctive neuroprotective treatments: arterial line filter Cognitive assessment follow-up time point: 4 months Study withdrawals, % (n/N): Unclear	Random sequence generation: low, computer-generated randomization Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: unclear, loss to follow-up NR Intention to Treat Analysis: unclear, loss to follow-up NR Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Kadoi, 2003[14] Location: Japan Funding Source: Non-industry	Inclusion Criteria: scheduled for elective CABG Exclusion Criteria: history of cerebrovascular disease, diabetes, psychiatric illness,	N=180 randomized, 152 completed 6-month tests) Age (yr): 65 Gender (Male %): 76 Race/Ethnicity (%): NR Education: NR	CV procedure: CABG with propofol infusion 4 to 6 mg per kg per hour for maintenance (n=90 randomized, 77 completed 6-month tests)	Random sequence generation: unclear, randomization method NR Allocation Concealment: unclear, NR

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
(Japanese Ministry of Science and Education) Study design: RCT	renal disease (creatinine concentration >2.0 mg/dL), or active liver disease (glutamine oxaloacetate transaminase or glutamine pyruvate transaminase > 40 U/dL); moderate or severe atherosclerotic lesions in the ascending aorta or carotid artery stenosis confirmed by pre-procedure ultrasonography and magnetic resonance imaging	Weight (kg): 62.5 BMI: 23.4 Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 0 (excluded) History of HTN (%): 65 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): NR History of Stroke (%): 0 (excluded) History of TIA (%):0 (excluded) History of PAD (%): NR Current smoker (%): 36 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	Control: CABG with fentanyl infusion 40 to 70 mcg/kg [time NR] for maintenance (n=90 randomized, 75 completed 6-month tests) **<u>Procedure characteristics</u>** Anesthesia type/duration: midazolam, fentanyl, and vecuronium for induction; vecuronium intermittently during maintenance/bypass time 130.5 min Adjunctive neuroprotective treatments: arterial line filter Cognitive assessment follow-up time point: 6 months Study withdrawals at 6 months, % (n/N): 16 (28/180) at 6 months	Masking outcomes assessment: low, outcome assessors were blinded to treatment group Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported by group Intention to Treat Analysis: no, completers- only analysis for 6-month cognitive outcomes Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Gold, 1995[15] Location: U.S. Funding Source: Non-industry (National Institutes of Health, National Heart, Lung, and Blood Institute) Study design: RCT	Inclusion Criteria: patients undergoing primary, nonemergency coronary bypass for left main or multivessel disease Exclusion Criteria: Inability to complete the neuropsychologic tests (blindness, deafness, language difficulties); participation in other studies; inability to return for follow-up	N=248 Age (yr): 66 Gender (Male %): 80 Race/Ethnicity (%): 93 Caucasian Education: 90% high school or higher Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 21 History of HTN (%): 50 History of CAD (%): 100 (presumed) History of CHF (%): 8 History of MI (%): 43	CV procedure: CABG with MAP during CBP maintained between 80 and 100 mm Hg (High MAP) (n=124) Control: CABG with MAP during CPB maintained between 50 and 60 mm Hg (low MAP) (n=124) **<u>Procedure characteristics</u>** Anesthesia type/duration: induction with thiopental and fentanyl; paralysis with pancuronium; maintenance with fentanyl, midazolam, or isoflurane/ bypass time 87 min	Random sequence generation: low, table of random numbers Allocation Concealment: unclear, NR Masking outcomes assessment: low, outcome assessors (cardiologist and neurologist) were blinded to the treatment group Attrition bias accounted for: low, numbers and reasons for loss to follow-up are described and are similar between groups Intention to Treat Analysis: unclear,

Appendix G. Table 1. Evidence table: Coronary Artery Bypass Grafting Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
		History of Stroke (%): 6 History of TIA (%): NR History of PAD (%): NR Current smoker (%): 6 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 7 days, 6 months. Study withdrawals, % (n/N): 9 (23/248) at 6 months	Trial describes itself as intent-to-treat analysis, but 6 month cognitive outcomes are actually a completers-only analysis; also reports pragmatic (ie, treatment-received) analysis for clinical outcomes Reporting bias from selective outcomes reporting: low, all prespecified outcomes are reported
Andrew, 2001[21] Location: Australia Funding Source: Non-industry (National Heart Foundation of Australia, Royal Australasian College of Surgeons) Study design: Prospective observational cohort study	Inclusion Criteria: elective cardiac surgery by either of 2 surgeons, operated on between January 1996 and November 1998, first language English Exclusion Criteria: previous cardiac surgery, history of a completed stroke	N=109 Age (yr): 66 Gender (Male %): 80 Race/Ethnicity (%): NR Education (y): 10.2 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%):18 History of HTN (%):47 History of CAD (%): 100 (presumed) History of CHF (%): NR History of MI (%): NR History of Stroke (%): 0 (excluded) History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV Procedure: CABG with multiple (≥3) grafts (extracardiac) (n= 59) Control: Isolated valve surgery or combined valve and coronary artery surgery (intracardiac) (n=50) **Procedure characteristics** Anesthesia type/duration: All patients received a standard moderate fentanyl-based anesthetic technique/bypass time 59.9 min Adjunctive neuroprotective treatments: NR Cognitive assessment follow-up time points: 7 days, 6 months Study withdrawals, % (n/N): 32 (35/109) at 6 months	Baseline groups similar in important prognostic indicators: low, groups are similar Attrition bias accounted for: low, patients unavailable for 6-month assessment did not significantly differ from the patients with complete data on demographic variables or the incidence of neuropsychologic deficits at 7-day assessment Masking outcomes assessment: unclear, NR Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

BMI = body mass index; BP = blood pressure; C=Celsius; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CECC= conventional extracorporeal circulation; CHF = congestive heart failure; CPB: cardiopulmonary bypass; CV = cardiovascular; dL=deciliter; DM = diabetes mellitus; HTN = hypertension; kg=killigrams; LDL = low density lipoprotein; MAP=mean arterial pressure; mcg/kg=micrograms per kilogram; mg=milligrams; MI = myocardial infarction; min=minutes; mm Hg: millimeters of mercury; MMSE=Mini Mental State Examination; µmol/L= micromoles per liter; n and N=number; NR = not reported; PAD = peripheral arterial disease; PMID=PubMed identifier; RCT = randomized controlled trial; TIA = transient ischemic attack; U=units; yr=year

Appendix G. Table 2. Evidence table: Aortic Valve Replacement Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
Knipp, 2013[23] Location: Germany Funding Source: NR Study design: Prospective observational cohort study	Inclusion Criteria: Transapical transcatheter aortic valve implantation (TA-TAVI): patients with severe symptomatic aortic stenosis deemed inoperable due to excessive high risk as estimated by the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) Exclusion Criteria: AVR: prior stroke or high-grade carotid stenosis, psychiatric or neurological illness requiring treatment, uncontrolled HTN, metabolic disease, alcoholism, non-fluency in the German language and acute endocarditis, patients who needed combined heart surgery (multiple valve disease, CAD, patent foramen ovale etc.) or heart and vascular surgery (ascending aortic aneurysm and carotid revascular-ization), criteria were contraindication to MRI scanning (e.g. pacemaker, claustrophobia) or emergencies.	N=64 Age (yr): TA-TAVI 82, AVR 68; p<0.001 Gender (Male %): TA-TAVI 26, AVR 51; p=0.04 Race/Ethnicity (%): NR Education (>8 y): TA-TAVI 15, AVR 32; p=0.07 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%):TA-TAVI 74, AVR 59; p=0.17 History of DM (%):TA-TAVI 30, AVR 8; p=0.03 History of HTN (%):TA-TAVI 100, AVR 76; p=0.01 History of CAD (%):TA-TAVI 56, AVR 0; p<0.001 History of CHF (%): NR History of MI (%): NR History of Stroke (%):TA-TAVI 22 "previous cerebral ischemic event," AVR 0 (excluded) History of TIA (%): *see above* History of PVD (%):TA-TAVI 30, AVR 3; p=0.01 Smoking (%):TA-TAVI 30, AVR 51; p<0.05 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	AVR (n=37) TA-TAVI (n=27) **<u>Procedure characteristics</u>** Anesthesia type/duration: NR Adjunctive <u>neuroprotective</u> treatments: Catheters and balloons were carefully deaired and guidewires thoroughly cleaned before use to minimize the risk of embolization. An aortic embolization protection filter was not used. Cognitive assessment follow-up time points: 3 months Study withdrawals: TA-TAVI: 33% (9/27) patients were not available for cognitive testing at followup versus 8% (3/37) for the AVR group. Mortality: TA-TAVI 25.9% (n=7) at 3 months versus 0% for AVR group.	Baseline groups similar in important prognostic indicators: high, groups had important differences in demographics and medical histories Attrition bias accounted for: high, numbers and reasons for loss to follow-up are described, but differ between groups Masking outcomes assessment: unclear, NR Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Fakin, 2012[18] Location: Austria, Switzerland Funding Source:	Inclusion Criteria: consecutive patients scheduled for elective biological AVR Exclusion Criteria: A history	N=60 Age (yr): 67 Gender (Male %): NR Race/Ethnicity (%): NR Education: NR Weight: NR	CV procedure: elective isolated biological AVR under hypothermia (32 °C) (n=30) Control: elective isolated biological AVR under	Random sequence generation: low, computer randomization Allocation Concealment: unclear, NR

Appendix G. Table 2. Evidence table: Aortic Valve Replacement Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	**Intervention/Duration**	**Risk of bias assessment** (Low, moderate, high, unclear)
NR Study design: RCT	of prior stroke with residual deficit, uncontrolled hypertension, carotid artery stenosis of 75% or greater, psychiatric illness requiring treatment, alcoholism; renal disease (creatinine more than 2.0 mg/dL [177 µmol/L]); or active liver disease	BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 33 History of HTN (%): NR History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	normothermia (37 °C) (n=30) **<u>Procedure characteristics</u>** Anesthesia type/duration: general anesthesia with midazolam, ethmidate, fentanyl and pancuronium and cardiopulmonary bypass/ bypass time 77 min Adjunctive <u>neuroprotective</u> treatments: NR Follow-up period: 4 months (mean) Cognitive assessment follow-up time point: 4 months Study withdrawals % (n/N): NR	Masking outcomes assessment: unclear, NR Attrition bias accounted for: unclear: NR Intention to Treat Analysis: unclear, NR Reporting bias from selective outcomes reporting: low, the one prespecified outcome was reported]
Andrew, 2001[21] Location: Australia Funding Source: Non-industry (National Heart Foundation of Australia, Royal Australasian College of Surgeons) Study design: Prospective observational cohort study	Inclusion Criteria: elective cardiac surgery by either of 2 surgeons, operated on between January 1996 and November 1998, first language English Exclusion Criteria: Previous cardiac surgery, history of a completed stroke	N=109 *Percents for groups reported for the variables considered unbalanced; Intracardiac=Int;Extracardiac=Ext)* Age (yr):65.5 Gender (Male %) : 79.8 Race/Ethnicity (%): NR Education (y): 10.2 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): NR History of DM (%): 17.6 *(Int 10 vs Ext 24)* History of HTN (%): 46.5 *(Int 40 vs Ext*	CV Procedure: Isolated valve surgery or combined valve surgery with CABG (intracardiac) (n= 50) Control: CABG with multiple (≥3) grafts (extracardiac) (n=59) **<u>Procedure characteristics</u>** Anesthesia type/duration: All patients received a standard moderate fentanyl-based anesthetic technique/bypass time 59.9 min Adjunctive <u>neuroprotective</u> treatments: NR	Baseline groups similar in important prognostic indicators: low, groups similar Attrition bias accounted for: low,patients unavailable for 6-month assessment did not significantly differ from the patients with complete data on demographic variables or the incidence of neuropsychologic deficits at 7-day assessment Masking outcomes assessment: unclear,NR Reporting bias from selective outcomes reporting: low, prespecified outcomes were

Appendix G. Table 2. Evidence table: Aortic Valve Replacement Studies

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
		52) History of CAD (%): NR History of CHF (%): NR History of MI (%): NR History of Stroke (%): 0 (excluded) History of TIA (%): NR History of PAD (%): NR Current smoker (%): NR Alcohol intake: NR Depression (%): NR Anxiety (%): NR	Follow-up period: 6 months Cognitive assessment follow-up time points: 6 months Study withdrawals, % (n/N): 32 (35/109) at 6 months	reported

AVR=aortic valve replacement; BMI = body mass index; BP = blood pressure; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CHF = congestive heart failure; CV = cardiovascular; DM = diabetes mellitus; HTN = hypertension; LDL = low density lipoprotein; mg/dL=milligrams per deciliter; MI = myocardial infarction; min=minutes; µmol/L= micromoles per liter; n and N=number; NR = not reported; PAD = peripheral arterial disease; RCT = randomized controlled trial; TIA = transient ischemic attack; yr=year

Appendix G. Table 3. Evidence table: Carotid Artery Stenting and Endarterectomy

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
Altinbas, 2011[16] Location: the Netherlands Funding Source: Non-Industry and industry (Netherlands Heart Foundation; Medical Research Council; the Stroke Association; Sanofi-Synthélabo; the European Union; the Swiss National Science Foundation; University of Basel; Reta Lila Weston Trust for Medical Research) Study design: RCT Note: some details from interim report, PMID 20189239	Inclusion Criteria: recent (within 12 months) symptomatic ICA stenosis of > 50% requiring treatment; older than 40 years Exclusion Criteria: major stroke without useful recovery of function, previous carotid endarterectomy or stenting in the randomized artery, contraindications for either treatment, or planned coronary artery bypass grafting or other major surgery	N=140 Age (yr): 69 Gender (Male %): 72 Race/Ethnicity (%): NR Education (median): 5.5 [units NR] Weight: NR BMI: NR Systolic BP (mm Hg): 168 Diastolic BP (mm Hg): 86.5 Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 70 History of DM (%): 21 History of HTN (%): 70 History of CAD (%): NR History of CHF (%): 3 History of MI (%): 16 History of Stroke (%): NR Recent ischemic stroke (%): 46 History of TIA (%): NR Recent TIA (%): 49 History of PAD (%): 16 Current smoker (%): 32 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: CAS; stents at physician's discretion and used in 90% (n=71 at baseline; n=61 at 6 month follow-up) Control: CEA using standard or eversion technique (n=69 at baseline; n =58 at 6 month follow-up) Local or general anesthesia, shunts, and patches at surgeon's discretion **Procedure characteristics** Anesthesia type/duration: general or local/ duration NR Adjunctive neuroprotective treatments: aspirin and clopidogrel for stenting; neuroprotective device recommended and used in 72% of CEA prodecures Follow-up period: 6 months Cognitive assessment follow-up time point: 6 months Study withdrawals, ie, no follow-up neuropsychiatric exam analyzed, % (n/N): 15 (21/140) at 6 months	Random sequence generation: low, computer randomization Allocation Concealment: low, by telephone or fax Masking outcomes assessment: high, outcome assessors were not masked to treatment assignment Attrition bias accounted for: low, numbers lost to follow-up appear similar between groups; patients who did not have 6 month neuropsychiatric exam were 6.2 yrs older but did not differ with regard to other demographic, clinical, or baseline cognitive characteristics; reasons for attrition are not reported by group Intention to Treat: no, analyzed by treatment received; completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported
Baracchini, 2012[22]	Inclusion Criteria, CEA intervention group: age 65	N=227 at baseline, 213 at 12 weeks (only completers reported)	CV procedure: Eversion CEA (n=145)	Baseline groups similar in important prognostic indicators: high,intervention group had non-

Appendix G. Table 3. Evidence table: Carotid Artery Stenting and Endarterectomy

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
Location: Italy Funding Source: NR Study design: Prospective observational cohort study	yrs or older; undergoing elective CEA under general anesthesia for symptomatic or asymptomatic severe (≥60% lumen reduction) carotid disease; history of TIA or minor stroke or asymptomatic Exclusion Criteria, CEA intervention group: dementia by DSM IV criteria and MMSE score < 24; major depressive disorder, bipolar disorder, or mental retardation according to DSM IV criteria; contralateral severe ICA stenosis or ICA occlusion; history of major stroke Inclusion Criteria, laparoscopic controls: undergoing laparoscopic cholecystectomy for gallbladder disease under general anesthesia during same time period, matched to intervention group by age and sex Exclusion Criteria, laparoscopic controls: history or clinical signs of neurologic or psychiatric disease, any evidence of cerebrovascular atherosclerosis (> 60%	*Percents for groups reported for the variables considered unbalanced; Sx=symptomatic; Asx=asymptomatic; Chol=cholecystectomy* Age (yr): 74 Gender (Male %): 71 Race/Ethnicity (%): NR Education (yr): 7.2 Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 44 History of DM (%): 36 *(Sx 33.3 vs Asx 34.3 vs Chol 41.2)* History of HTN (%): 58 *(Sx 60 vs Asx 58.6 vs Chol 54.4)* History of CAD (%): 39 *(Sx 42.6 vs Asx 38.6 vs Chol 33.8)* History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of TIA (%): NR History of PAD (%): NR Current smoker (%): 66.7 *(Sx 69.3 vs Asx 70.0 vs Chol 60.3)* Alcohol intake: NR Depression (%): NR Anxiety (%): NR	Control: laparoscopic cholecystectomy under (n=68) **Procedure characteristics** Anesthesia type/duration: CEA: general anesthesia with EEG monitoring / 46 min; cholecystectomy: general anesthesia / duration NR Adjunctive neuroprotective treatments: NR Follow-up period: mean: 3 months (94 days) and 12 months (14.2 months) Cognitive assessment follow-up time points: 3 and 12 months Study withdrawals, % (n/N): 6 (14/227) at 12 months	significantly worse prognostic factors in hypertension, smoking, cardiac disease, but non-significantly better prognostic factor in diabetes mellitus; analysis did not adjust for differences in prognostic factors Attrition bias accounted for: high, numbers and reasons for loss to follow-up are not described by groups Masking outcomes assessment: moderate, outcome assessor was masked to whether patients were asx or sx and to previous test results; whether outcome assessor was masked to cholecystectomy or CEA group NR Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix G. Table 3. Evidence table: Carotid Artery Stenting and Endarterectomy

Study/Location/ Funding Source/Study design	Inclusion/Exclusion Criteria	**Patient Characteristics** (expressed in means unless otherwise noted)	Intervention/Duration	**Risk of bias assessment** (Low, moderate, high, unclear)
	stenosis) by TCDS			
Crawley, 2000[17] Location: United Kingdom Funding Source: Non-Industry (UK [North Thames] National Health Service [NHS] Research and Development grant; NHS Management Executive grant; British Heart Foundation; Wellcome Trust; Neurosciences Research Foundation) Study design: RCT (96% of subjects were a subgroup of RCT) Note: some details from earlier, full report of CAVATAS trial PMID 11403808	Inclusion Criteria: severe (>70%) symptomatic carotid stenosis suitable for either carotid endarterectomy or endovascular treatment Exclusion Criteria: patient refusal or inability to obtain a TCD signal; disabling stroke, recent myocardial infarction, poorly controlled hypertension or diabetes mellitus, renal disease, respiratory failure, inaccessible carotid stenosis, or severe cervical spondylosis	N= 46 Age (yr): 68 Gender (Male %): 74 Race/Ethnicity (%): NR Education: NR Weight: NR BMI: NR Systolic BP (mm Hg): NR Diastolic BP (mm Hg): NR Total cholesterol (mg/dL): NR LDL cholesterol (mg/dL): NR Dyslipidemia (%): 59 History of DM (%): 7 History of HTN (%): 57 History of CAD (%): 37 History of CHF (%): NR History of MI (%): NR History of Stroke (%): NR History of TIA (%): NR History of PAD (%): 20 Current smoker (%):26 Alcohol intake: NR Depression (%): NR Anxiety (%): NR	CV procedure: carotid PTA using access through femoral artery; balloon angioplasty with TCD monitoring; 1 patient also had stenting (n=20) Control: CEA under general anesthesia with TCD monitoring (n=26) **Procedure characteristics** Anesthesia type/duration: CEA under general anesthesia; carotid PTA NR/ duration NR Adjunctive neuroprotective treatments: For CEA: flow directed into the external carotid on restitution of flow (to minimize passage of debris into the cerebral circulation) Follow-up period: 6 weeks, 6 months Cognitive assessment follow-up time points: 6 weeks, 6 months Study withdrawals, % (n/N): 2 (1/46) at 6 weeks, 13 (6/46) at 6 months	Random sequence generation: low, computer randomization Allocation Concealment: low, by telephone call or fax to the randomization center Masking outcomes assessment: moderate, outcome assessor was masked to procedure Attrition bias accounted for: unclear, numbers lost to follow-up appear similar between groups, but reasons for attrition are not reported by group Intention to Treat Analysis: no, completers-only analysis Reporting bias from selective outcomes reporting: low, all prespecified outcomes were reported

Appendix H

Cognitive Outcomes Tables:
Clinically Diagnosed Cognitive Impairment

Appendix H. Table 1. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment - CABG

Study	Confirmed symptomatic CI* associated with functional impairment (n/N) %				Confirmed symptomatic CI* not associated with functional impairment, clinically diagnosed (n/N) %			
	Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/	NR	NR	NR	NR	NR	NR	NR	NR
Jensen, 2006;[24] 2008[2] Off-pump CABG (n=61) vs. On-pump CABG (n=59)	NR	NR	NR	NR	NR	NR	NR	NR
Vedin, 2006[3] Off-pump CABG (n=33) vs. On-pump CABG (n=37)	NR	NR	NR	NR	NR	NR	NR	NR
Lund, 2005[4] Off-pump CABG (n=60) vs. On-pump CABG (n=60)	NR	NR	NR	NR	NR	NR	NR	NR
Lee, 2003[5] Off-pump CABG (n=30) vs. On-pump (n=30)	NR	NR	NR	NR	NR	NR	NR	NR
Selnes, 2009[20] Off-pump CABG (n=75) vs. On-pump CABG (n=152)	NR	NR	NR	NR	NR	NR	NR	NR
Selnes, 2009[20] Off-pump CABG (n=75) vs. Non-surgical control (n=99)/	NR	NR	NR	NR	NR	NR	NR	NR
Selnes, 2009[20] On-pump CABG (n=152) vs. Non-surgical control	NR	NR	NR	NR	NR	NR	NR	NR

Appendix H. Table 1. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment - CABG

(n=99)								
Boodhwani, 2007[6] Normothermic (n=134) vs. Hypothermic [n=133])	NR	NR	NR	NR	NR	NR	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) vs. Hypothermic (n=111)	NR	NR	NR	NR	NR	NR	NR	NR
Djaiani, 2012[9] Cell-saver (n=84) vs. Control (n=86)	NR	NR	NR	NR	NR	NR	NR	NR
Anastasiadis 2011;[10] MECC (n=32) vs. CECC (n=32)	NR	NR	NR	NR	NR	NR	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53)	NR	NR	NR	NR	NR	NR	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170)	NR	NR	NR	NR	NR	NR	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)	NR	NR	NR	NR	NR	NR	NR	NR

Appendix H. Table 1. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment - CABG

Kadoi, 2003[27] CABG with propofol (n=90) vs CABG with fentanyl (n=90)	NR	NR	NR	NR	NR	NR	NR	NR
Gold, 1995[15] Low MAP (n=124) vs. High MAP (n=124)	NR	NR	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Extracardiac (n=59) vs. Intracardiac (n=50)	NR	NR	NR	NR	NR	NR	NR	NR

CI = cognitive impairment; NR = not reported; MECC = minimal extracorporeal circulation; CECC = conventional extracorporeal circulation

Appendix H. Table 2. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment - AVR

Study	Confirmed symptomatic CI associated with functional impairment (n/N) %				Confirmed symptomatic CI not associated with functional impairment, clinically diagnosed (n/N) %			
	Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) vs. TA-TAVI (n=27)								
Fakin, 2011[18] Hypothermic AVR (n=30) vs. Normothermic (n=30)	NR	NR	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)	NR	NR	NR	NR	NR	NR	NR	NR

CI = cognitive impairment; NR = not reported; TA-TAVI = transapical transcatheter aortic valve implantation

Appendix H. Table 3. Cognitive Outcomes Tables: Clinically Diagnosed Cognitive Impairment – CAS and CEA

Study	Confirmed symptomatic CI associated with functional impairment (n/N) %				Confirmed symptomatic CI <u>not</u> associated with functional impairment, clinically diagnosed (n/N) %			
	Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69)	NR	NR	NR	NR	NR	NR	NR	NR
Baracchini, 2012[22]CEA (n=145) vs. Laparoscopic cholecystectomy Control (n=68)	NR	NR	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26)	NR	NR	NR	NR	NR	NR	NR	NR

CI = cognitive impairment; NIHSS= National Institutes of Health Stroke Scale; NR = not reported; PTA=percutaneous transluminal angioplasty; RCT=raandomized controlled trial

Appendix I

Cognitive Outcomes Tables:
Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests

Appendix I. Table 1. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - CABG

Study/ Design	Neuropsychological composite cognitive impairment (CI) n/N (%)					
	Pre-Procedure cognitive status		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	NR	NR	NR	NR	NR	NR
Jensen, 2006;[24] 2008[2] Off-pump CABG (n=61) vs. On-pump CABG (n=59)/ RCT	All subjects had MMSE >24 (score ≥25 points out of 30 indicates a normal cognition)	All subjects had MMSE >24	<u>3 months</u> Definition 1 4/54 (7.4) RR 0.76 [0.21 to 2.66]; P=0.66 Definition 2 11/54 (20.4) RR 0.87 [0.42 to 1.78]; P=0.70 Definition 3 14/54 (26.0) RR 1.20 [0.60 to 2.40]; P=0.60 <u>12 months</u> Definition 1 9/47 (19.1) RR 2.06 [0.68 to 6.20]; P=0.20 Definition 2 6/47 (12.8) RR 1.10 [0.36 to 3.34]; P=0.87 Definition 3 14/47 (29.8) RR 1.07 [0.56 to 2.05]; P=0.84	<u>3 months</u> Definition 1 5/51 (9.8) Definition 2 12/51 (23.5) Definition 3 11/51 (21.6) <u>12 months</u> Definition 1 4/43 (9.3) Definition 2 5/43 (11.6) Definition 3 12/43 (27.9)	NR	NR
Vedin, 2006[3] Off-pump CABG (n=33) vs. On-pump CABG (n=37) / RCT	NR	NR	<u>6 months</u> 5/33 (15) RR 0.80 [0.28 to 2.28]; P=0.68	<u>6 months</u> 7/37 (19)	NR	NR
Lund, 2005[4] Off-pump CABG	NR	NR	<u>3 months</u> 11/54 (20.4)	<u>3 months</u> 12/52 (23.1)	NR	NR

Appendix I. Table 1. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - CABG

Study/ Design	Neuropsychological composite cognitive impairment (CI) n/N (%)					
	Pre-Procedure cognitive status		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control
(n=60) vs. On-pump CABG (n=60) / RCT			RR 0.88 [0.43 to 1.82]; P=0.74 12 months 13/54 (24.1) 1.04 [0.53 to 2.07]; P=0.90	12 months 12/52 (23.1)		
Lee, 2003[5] Off-pump CABG (n=30) vs. On-pump (n=30) / RCT	NR	NR	12 months 5/27 (18.5) RR 1.25 [0.38 to 4.16]; P=0.72	12 months 4/27 (14.8)	NR	NR
Selnes, 2009;[20] McKhann, 2005[28] Off-pump CABG (n=75) vs. On-pump CABG (n=152) / Prosp.	Mean MMSE = 27.7; 4.2% had a MMSE score <24	Mean MMSE = 27.6; 4.6% had a MMSE score <24	NR	NR	NR	NR
Selnes, 2009;[20] McKhann, 2005[28] Off-pump CABG (n=75) vs. Non-surgical control (n=99)/ Prosp.	Mean MMSE = 27.7; 4.2% had a MMSE score <24	Mean MMSE = 27.9; 6.1% had a MMSE score <24	NR	NR	NR	NR
Selnes, 2009[20]/ McKhann, 2005[28] On-pump CABG (n=152) vs. Non-surgical control (n=99)/ Prosp.	Mean MMSE = 27.6; 4.6% had a MMSE score <24	Mean MMSE = 27.9; 6.1% had a MMSE score <24	NR	NR	NR	NR
Boodhwani, 2007[6] Normothermic (n=134) versus Hypothermic (n=133)/ RCT	NR	NR	3 months n/N, NR (4)	3 months n/N, NR (8)	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) versus Hypothermic	NR	NR	NR	NR	5 years 27/65 (42) RR 0.95 [0.64 to 1.41]; P=0.78	5 years 29/66 (44)

Appendix I. Table 1. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - CABG

Study/ Design	Neuropsychological composite cognitive impairment (CI) n/N (%)					
	Pre-Procedure cognitive status		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control
(n=111)/ RCT						
Djaiani, 2012[9] Cell-saver (n=84) vs. Control (n=86)/ RCT	NR	NR	NR	NR	1 year 16/84 (19.0) RR 1.09 [0.58 to 2.06]; P=0.79	1 year 15/86 (17.4)
Anastasiadis, 2011[10] MECC (n=32) vs. CECC (n=32) / RCT	NR	NR	3 months 6/29 (21) RR 0.34 [0.16 to 0.73]; P=0.005	3 months 19/31 (61)	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53)/ RCT	NR	NR	NR	NR	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170) / RCT	NR	NR	12 months† 20% rule: 42/159 (26) RR 1.10 [0.74 to 1.62]; P=0.65 1 SD rule: 24/159 (15) RR 1.18 [0.67 to 2.09]; P=0.56	12 months† 20% rule: 34/141 (24) 1 SD rule: 18/141 (13)	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)/ RCT	NR	NR	4 months 9/33 (27.3) RR 0.53 [0.27 to 1.02]; P=0.06	4 months 16/31 (51.6)	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90)/ RCT	NR	NR	6 months: 5/77 (6) RR 0.97 [0.29 to 3.23]; P=0.97	6 months: 5/75 (7)	NR	NR
Gold, 1995[15]			6 months	6 months		

Appendix I. Table 1. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - CABG

Study/ Design	Neuropsychological composite cognitive impairment (CI) n/N (%)					
	Pre-Procedure cognitive status		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control
Low MAP (n=124) vs. High MAP (n=124)/ RCT	NR	NR	n/N, NR (11)	n/N, NR (12)	NR	NR
Andrew, 2001[21] Extracardiac (n=59) vs. Intra-cardiac (n=50)	NR	NR	NR	NR	NR	NR

CI = cognitive impairment; MMSE = Mini–mental state examination; NR = not reported; RR = risk ratio [95% confidence intervals]
* Decision to participate in neurocognitive testing was optional but decided prior to randomization to avoid biases.

Neuropsychological composite cognitive impairment outcomes definitions:
Jensen 2006: There were 3 definitions

1) occurrence of at least 2 of 7 possible deficits in A) Visual Verbal Learning; B) Concept Shifting Task; C) Stroop Color Word Interference; and D) Letter-Digit Coding. The 7 possible deficits were 2 possible deficits in A, B, and C and 1 possible deficit in D. For the 2 error scores, a deficit was defined as ≥4 additional errors postoperatively compared with Pre-Procedurely out of 16 possible in B and ≥5 additional errors postoperatively compared with Pre-Procedurely out of 40 possible in C.
2) 20% decline in cognitive scores compared with baseline.
3) International Study of Post-Operative Cognitive Dysfunction definition, in which changes in the performance of 7 parameters from the result of the 4 tests were calculated. For each individual test outcome, the average learning effect was subtracted from these changes, and a *z* score was obtained after division by the SD from an age-matched healthy control group. When 2 of 7 *z* scores in individual tests or the combined *z* score were 1.96 or more, patients were defined as having cognitive dysfunction.

Vedin 2006: 20% decline in 20% (or two) of the cognitive tests (Digit Span, Block Span, Trail-Making Test A—D, Digit-symbol, COWAT-FAS, Claeson-Dahl Verbal Learning Test & Claeson-Dahl Verbal Retention Test) according to 'Statement of Consensus on Assessment of Neurobehavioral Outcomes after Cardiac Surgery.'

Lund 2005: >20% decrease on at least two tests (Grooved Pegboard Test, Digit Symbol [WAIS-R], Trail Making Test, Digit Span [WAIS-R], Stroop Color-Word Interference Test, Rey Auditory Verbal Learning Test, L and R, Similarities [WAIS-R], Controlled Oral Association Test [COWAT]), and Block Design [WAIS-R] at the 3- or the 12-month control compared with the Pre-Procedure assessment were defined as cognitively impaired.

Lee 2003: 20% decline in 20% (or two) of the cognitive tests (Vocabulary subtest Wechsler Adult Intelligence Scale (WAIS III), Rey Auditory Verbal Learning Test, Benton Visual Retention Test, Trail Making Test, Parts A and B, Grooved Pegboard Test, Finger Tapping Test, Digit Symbol subtest of the WAIS III), using the recommended core neuropsychological battery according to the 1994 Conference on CNS Dysfunction.

Boodhwani, 2007 Deficit was prospectively defined as a 1 standard deviation decrease in individual scores from baseline in 1 or more domains. *RAVLT*, Rey Auditory Verbal Learning Test; *WMS*, Wechsler Memory Scale; *SDMT*, Symbol Digit Modalities Test.

Nathan 2001, 2007 A patient was classified as having a cognitive deficit if a decrease of ≥ 0.50 SD was realized in 1 or more domains.

Djaiani, 2012 Patients with a negative score of\1 were considered to have POCD

Anastasiadis 2011: Cognitive decline defined as a decline of 1 SD or more (based on normative data relative to Pre-Procedure performance) in one ormore of the neurocognitive tests.

Silbert 2006: Two or more abnormal test results based on 1) "20% rule": decrease of 20% for each individual from baseline (per Rasmussen et al NNewman et al) or on 2) "1 SD rule": a decrease of an individual's score of at least 1 standard deviation of the baseline mean for all patients for the relevant test (per Keizer et al and Lewis et al)

Appendix I. Table 1. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - CABG

Alex, 2005 A postoperative deterioration of greater than 1 SD from the Pre-Procedure score in 2 or more tests (28% of the tests) was considered significant neuropsychometric impairment. (Tests included: the adult memory and information-processing table A, digit span forward, and digit span backward, in addition to the 4 recommended core tests [trail making A, trail making B, grooved peg board, and the Rey auditory verbal learning test.])

Kadoi 2003: “Significant impairment” was defined as a decline from Pre-Procedure testing of more than one standard deviation on more than 20% of test measures (at least two of six tests: Mini-Mental Test, Rey Auditory Verbal Learning Test, (3) Trail-Making Test (part A), Trail-Making Test (part B), digit span forward, or grooved pegboard).

Gold, 1995 Deterioration on three or more cognitive tests was defined as a cognitive complication.

† Silbert also reported composite outcomes at 3 months

Appendix I. Table 2. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests - AVR

Study	Neuropsychological composite cognitive impairment (CI) (n/N) %					
	Pre-Procedure Cognitive Status		Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) vs. TA-TAVI (n=27)	NR	NR	3 months 2/34 (6) P=0.04	3 months 5/18 (28)	NR	NR
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30)	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)	NR	NR	NR	NR	NR	NR

CI = cognitive impairment; NR = not reported; TA-TAVI = transapical transcatheter aortic valve implantation

Neuropsychological composite cognitive impairment outcomes definitions:

1. Knipp 2013 – a cognitive composite test score (defined as difference between the number of tests with improvement and decline) of ≤−2 in TA-TAVI patients and ≤−3 in AVR patients denoted a clinically significant cognitive decline in the individual patient.
2. Fakin, 2011 – reported correlation between neurocognitive brain function measured by P300 auditory evoked potentials between pre-procedure and 4 months (repeated measures analysis of variance)

Appendix I. Table 3. Cognitive Outcomes Tables: Incident Cognitive Impairment Defined by Composite of Neuropsychological Tests – CAS and CEA

Study	Neuropsychological composite cognitive impairment (CI) (n/N) %			
	Intermediate-term (3-12 months) follow-up		Long-term (>12 months) follow-up	
	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs CEA (n=69) RCT	NR	NR	NR	NR
Baracchini, 2012[22] CEA (n=145) vs. Laparoscopic cholecystectomy Control (n=68) Prospective observational cohort study	NR	NR	NR	NR
Crawley, 2000[17] CEA (n=26) vs carotid PTA (n=20) RCT	6 months 4/22 (18) RR 0.47 [0.16 to 1.35]; P=0.16	6 months 7/18 (38)	NR	NR

CI = cognitive impairment; NR = not reported; PTA: percutaneous transluminal angiography; RR = risk ratio [95% confidence intervals]

Neuropsychological composite cognitive impairment outcomes definitions:
Crawley 2000: A drop in the postoperative score by ≥ 1 SD from the pre-procedure score.

Appendix J

Cognitive Outcomes Tables:
Individual Neuropsychological Tests/Cognitive Domains

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG
Attention Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	Digit Symbol Substitution Test (WAIS)	33.0 (17.8);n=989*	31.9 (18.0); n=986*	30 days, change 1.8 (11.4); n=694*	30 days, change 1.3 (10.8); n=685*	1 year, change 1.8 (13.2); n=522*	1 year, change 1.3 (12.3); n=528*
Jensen, 2006;[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	Trail Making A (s)	34 (30-38);* n=33	37 (31-42);* n=37	6 mos., all 32 (29-35);* n=30	6 mos., all 34 (32-37);* n=32	NR	NR
	Digit Span (WAIS-R), forward	7.4 (6.8-8.0);* n=33	7.1 (6.3-7.8;);* n=37	7.2 (6.8-7.6);* n=30	7.2 (6.5-7.8);* n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	Digit Span (WAIS-R)	9.8 (1.4) n=60	10.4 (2.0) n=60	12 mos. † 9.9 (1.6) n=54	12 mos. † 10.8 (3.5) n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT	Trail Making A (s)	47.4 (22.2); n=30	43.7 (32.6); n=30	12 mos. 45.7 (15.2); n=27	12 mos. 43.4 (34.4); n=26	NR	NR
Selnes, 2009[20] CABG (Off) (n=75) vs. CABG (On) (n=152)/ Prospective	Trail Making A (s)	48.0 (23.0); n=69	47.1 (24.2); n=151	12 mos., all ** 43.4 (17.5); n=55	12 mos., all ** 40.8 (16.8); n=123	72 mos., all 42.6 (15.9); n=43	72 mos., all 47.7 (29.5); n=95
	MMSE- attention	4.2 (1.1); n=72	4.0 (1.3); n=152	4.0 (1.0); n=55	4.0 (1.0); n=124	4.3 (1.0); n=43	4.0 (1.3); n=96
Selnes, 2009[20] CABG (Off) (n=75) vs. Non-surgical control (n=99)/ Prospective	Trail Making A (s)	48.0 (23.0); n=69	43.1 (14.4); n=99	12 mos., all ** 43.4 (17.5); n=55	12 mos., all ** 41.0 (15.6); n=91	72 mos., all 42.6 (15.9); n=43	72 mos., all 46.4 (31.6); n=67
	MMSE- attention	4.2 (1.1); n=72	4.2 (1.2); n=99	4.0 (1.0); n=55	5.0 (1.0); n=91	4.3 (1.0); n=43	4.3 (1.2); n=67
Selnes, 2009[20] CABG (On) (n=152) vs. Non-surgical control	Trail Making A (s)	47.1 (24.2); n=151	43.1 (14.4); n=99	12 mos., all ** 40.8 (16.8); n=123	12 mos., all ** 41.0 (15.6); n=91	72 mos., all 47.7 (29.5); n=95	72 mos., all 46.4 (31.6); n=67

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
(n=99)/ Prospective	MMSE- attention	4.0 (1.3); n=152	4.2 (1.2); n=99	4.0 (1.0); n=124	5.0 (1.0); n=91	4.0 (1.3); n=96	4.3 (1.2); n=67
Boodhwani, 2007[6] Hypothermic (n=133) vs. Normothermic (n=134) / RCT	Digit span backward (Digback)	score 6.1 (2.1)	score 6.3 (2.1)	3 months, all change 0.5 (1.9) n=119	3 months, all change -0.3 (1.7) n=117	NR	NR
	Digit span forward (Digfor)	9.7 (2.2)	9.6 (2.0))	change 0.3 (1.7) n=119	change 0.3 (1.8) n=117	NR	NR
	Wechsler memory Scale (WMS) Mental Control	24.2 (5.5)	24.7 (5.2)	change 1.5 (3.3) n=119	change 0.7 (4.0) n=117	NR	NR
	Trail Making A	41.9 (14.8)	40.2 (12.3)	-4.0 (12.3) n=119	-1.4 (11.9) n=117	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) vs. Hypothermic (n=111)/ RCT	Digital Span Forward	7.2 (2.5) all 5-yr completers: 7.3 (2.5)	8.0 (2.2) all 5-yr completers: 8.2(2.3)	NR	NR	5 years, all Change −0.6 (1.5) n=65	5 years, all Change −0.3 (2.0) n=66
	Digital Span Backward	5.9 (2.4) all 5-yr completers: 6.2 (2.4)	6.7 (2.5) all 5-yr completers: 6.8 (2.7)	NR	NR	Change −0.1 (1.9) n=65	Change −0.1 (2.2) n=66
Djaiani, 2012[9] Cell-saver (n=84) vs. suction control (n=86)/ RCT	Digital Span Forward	10.13 (2.42)	10.20 (2.04)	1 year, all 10.9 (2.39) n=83	1 year, all 10.46 (1.81) n=82	NR	NR
	Choice Reaction Time / simple Reaction Time	414.18 (107.54)	446.44 (120.17)	408.42 (110.95) n=84	423.96 (122.93) n=86	NR	NR
Anastasiadis 2011;[10] MECC (n=32) vs. CECC (n=32) / RCT	Digit Span, forward	6.5 (1.5); n=32	6.7 (2.1); n=32	3 mos., all 6.9 (1.8); n=29	3 mos., all 6.3 (1.5); n=31	NR	NR
	Digit Symbol Modalities Test	36.7 (15.9); n=32	29.7 (17.2); n=32	43.2 (17.1); n=29	24.2 (17.7); n=31	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53) / RCT	Trail Making A (s)	43.19 (10.93)	42.59 (10.71)	3 months, all 44.09 (14.54); n=43	3 months, all 47.21 (10.10); n=44	NR	NR
	WAIS digit span forwards	48.84 (10.12)	50.02 (10.98)	47.91 (9.22); n=43	50.79 (10.72) n=44	NR	NR
	Zimmermann and Fimm Change of reaction, median reaction time	37.95 (10.66)	38.25(12.69)	44.10 (12.47); n=43	43.90 (14.16); n=44	NR	NR
	Zimmermann and Fimm Change of reaction, SD of	42.26 (13.99)	45.77 (17.82)	53.13 (18.90); n=43	53.55 (19.72); n=44	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	reaction time						
	Zimmermann and Fimm Divided attention t, median reaction time	47.73 (10.59)	43.44 (10.94)	46.74 (10.89); n=43	46.07 (8.82); n=44	NR	NR
	Zimmermann and Fimm Divided attention, SD of reaction time	47.73 (9.43)	45.30 (9.20)	50.32 (7.38); n=43	52.04 (7.43); n=44	NR	NR
	Digit–Symbol Substitution Test	34.8 (9.7)	33.7 (10.3)	38.9 (10.9); n=159	37.1 (10.9); n=141	NR	NR
	Trail Making A (s)	55.0 (25.7)	54.6 (23.6)	48.0 (18.1); n=159	50.8 (22.6); n=141	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. hyperbaric oxygen (n=33)/ RCT	Trail making A (s)	43 (16.3)	41.7 (14.9)	4 months, all 41.4 (15.5) n=33	4 months, all 40.6 (15.7) n=31	NR	NR
	Digit Span Forward	8.9 (2.3)	9.9 (2.7)	9.2 (2.5) N=33	9.5 (2.6) n=31	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90)/ RCT	Trail Making A	42.5 (6.6)	43.2 (5.6)	6 months 44.1 (5.7) n=77	6 months 45.4 (6.9) n=75	NR	NR
	Digit span forward	7.6 (2.0)	7.5 (2.2)	8.0 (2.2)	7.7 (2.4)	NR	NR
Gold, 1995#[15] Low MAP (n=124) versus High MAP (n=124) / RCT	Trail Making A	43.7 (22.3)	45.2 (24.7)	6 months, all change -2.7 (15.4) n=113	6 months, all change -4.0 (20.3) n=112	NR	NR
Andrew, 2001[21] Extracardiac (n=59) vs. Intracardiac (n=50)/ RCT	Trail Making A	40.8 (15.7)	44.5 (17.3)	6 months 25.0% with deficit n=44	6 months 33.3% with deficit n=30	NR	NR

* Decision to participate in neurocognitive testing was optional but decided prior to randomization to avoid biases.

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG
Executive Function Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	Trail Making B (s)	158.0 (88.1); n=721*	163.7 (89.5); n=711*	30 days, change -10.9 (58.1); n=470*	30 days, change -4.7 (71.2); n=487*	1 year, change -6.8 (64.0); n=353*	1 year, change -3.2 (70.2); n=340*
Jensen, 2006[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	Stroop Color-Word Test, time, part 3 (s)	64.8 (18.7); n=61	72.1 (27.7); n=59	12 mos., all 65.2 (20.6); n=47	12 mos., all 66.7 (21.2); n=43	NR	NR
	Stroop Color-Word Test, number of errors, part 3	2.6 (3.2); n=61	3.0 (4.2); n=59	2.4 (3.7); n=47	1.7 (2.6); n=43	NR	NR
	Concept Shifting Test, part C (s)	61.7(24.9); n=61	63.6 (23.4); n=59	66.7 (27.0); n=47	64.4 (25.1); n=43	NR	NR
	Concept Shifting Test, number of errors, part C	1.8 (2.7); n=61	0.9 (1.7); n=59	2.2 (2.5); n=47	1.8 (2.5); n=43	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	Trail Making B (s)	82 (72-92)* n=33	104 (86-122)* n=37	6 mos., all 84 (80-87)* n=30	6 mos., all 83 (74-92)* n=32	NR	NR
	Digit Span (WAIS-R), backward	6.2 (5.6-6.7)* n=33	5.6 (5.1-6.2)* n=37	6.7 (6.2-7.3)* n=30	6.2 (5.8-6.5)* n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	Stroop Color-Word Interference Test (s)	73.2 (31.7); n=60	75.4 (43.5); n=60	12 mos. † 69.9 (31.1); n=54	12 mos. † 69.5 (26.5); n=52	NR	NR
	Trail Making, Part B – Part A (s)	68.3 (30.9); n=60	65.3 (41.9); n=60	63.2 (37.5); n=54	60.4 (37.4); n=52	NR	NR
	Similarities (WAIS-R), raw score	18.2 (4.4); n=60	18.7 (3.9); n=60	19.7 (4.5); n=54	20.5 (3.8); n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT	Trail Making B (s)	126.0 (86.7); n=30	114.9 (87.6); n=30	12 mos. 117.3 (63.4); n=27	12 mos. 104.4 (92.1); n=26	NR	NR
Selnes, 2009[20] CABG (Off) (n=75) vs. CABG (on) (n=152)/ Prospective	Trail Making B (s)	96.9 (34.7) n=68	105.2 (59.0); n=147	12 mos., all** 97.2 (48.4) n=55	12 mos., all** 95.4 (48.2) n=122	72 mos., all 101.1 (47.1) n=43	72 mos., all 105.0 (50.1); n=91
	Rey Complex Figure, copy	32.6 (4.0); n=71	32.5 (4.7); n=152	33.4 (3.4); n=55	33.1 (3.6); n=124	32.5 (3.9); n=43	31.4 (5.2); n=94
Selnes, 2009[20] CABG (Off) (n=75)	Trail Making B (s)	96.9 (34.7) n=68	95.4 (40.0) n=99	12 mos., all** 97.2 (48.4) n=55	12 mos., all** 92.0 (41.5) n=91	72 mos., all 101.1 (47.1) n=43	72 mos., all 100.4 (50.6) n=66

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
vs. Non-surgical control (n=99)/ Prospective	Rey Complex Figure, copy	32.6 (4.0); n=71	33.0 (3.2); n=99	33.4 (3.4); n=55	33.0 (3.4); n=91	32.5 (3.9); n=43	32.4 (3.4); n=65
Selnes, 2009[20] CABG (On) (n=152) vs. Non-surgical control (n=99)/ Prospective	Trail Making B (s)	105.2 (59.0); n=147	95.4 (40.0) n=99	12 mos., all** 95.4 (48.2) n=122	12 mos., all** 92.0 (41.5) n=91	72 mos., all 105.0 (50.1); n=91	72 mos., all 100.4 (50.6) n=66
	Rey Complex Figure, copy	32.5 (4.7); n=152	33.0 (3.2); n=99	33.1 (3.6); n=124	33.0 (3.4); n=91	31.4 (5.2); n=94	32.4 (3.4); n=65
Boodhwani, 2007[6] Hypothermic (n=133) vs. Normothermic (n=134) / RCT	Letter fluency	31.7 (12.1)	32.2 (12.4)	3 months, all change 2.6 (7.2) n=119	3 months, all change 1.0 (8.1) n=117	NR	NR
	Trail Making B (s)	105.6 (45.0)	103.3 (43.3)	-11.7 (29.0) n=119	-7.8 (35.5) n=117	NR	NR
	Digit span backward (Digback)	6.1 (2.1)	6.3 (2.1)	0.5 (1.9) n=119	-0.3 (1.7) n=117	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) vs. Hypothermic (n=111)/ RCT	Trail Making B (s)	109 (47.7) all 5-yr completers: 104.3 (46.7)	106 (50.3) all 5-yr completers: 103.7 (9.2)	NR	NR	5 years change 24.2 (47.8) n=65	5 years change 14.1 (43.6) n=66
	Digital Span Backward	5.9 (2.4) all 5-yr completers: 6.2 (2.4)	6.7 (2.5) all 5-yr completers: 6.8 (2.7)	NR	NR	Change −0.1 (1.9) n=65	Change −0.1 (2.2) n=66
Djaiani, 2012[9] Cell-saver (n=84) vs. Suction control (n=86)/ RCT	Digital Span Backward	6.30 (2.25)	6.39 (2.46)	1 year, all 6.70 (2.54) N=84	1 year, all 6.24 (2.08) N=85	NR	NR
	Trails B-A (s)	53.31 (34.60)	54.26 (35.21)	50.2 (33.2) n=83	49.96 (31.8)n=83	NR	NR
Anastasiadis, 2011[10] MECC (n=32) vs. CECC (n=32) / RCT	Stroop Color-Word	34 (13); n=32	29 (9.3); n=32	3 mos., all 39.5 (14); n=29	3 mos., all 28.4 (10.5); n=31	NR	NR
	Digit Symbol Modalities Test	36.7 (15.9); n=32	29.7 (17.2); n=32	43.2 (17.1); n=29	24.2 (17.7); n=31	NR	NR
	Digit Span (WAIS-R), backward	4.3 (1.6); n=32	4.1 (1.5); n=32	4.7 (1.4); n=29	3.5 (1.1); n=31	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53) /	Trail making test B (s)	40.53 (10.09)	40.66 (10.92)	3 months, all 44.81 (11.34); n=43	3 months, all 45.45 (12.84); n=44	NR	NR
	Digit span, backward	47.00 (10.00)	47.80 (10.40)	46.69 (8.51); n=43	47.11(10.00); n=44	NR	NR
	Horn's performance test, subtest III	52.84 (7.29)	50.77 (8.39)	56.38 (8.85); n=43	54.48 (8.47); n=44	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
RCT	Zimmermann and Fimm Divided attention t, median reaction time	47.73 (10.59)	43.44 (10.94)	46.74 (10.89); n=43	46.07 (8.82); n=44	NR	NR
	Zimmermann and Fimm Divided attention, SD of reaction time	47.73 (9.43)	45.30 (9.20)	50.32 (7.38); n=43	52.04 (7.43); n=44	NR	NR
	Controlled Oral Word Association Test	33.1 (12.3)	31.4 (11.3	35.3 (12.0); n=159	33.4 (12.9); n=141	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170) / RCT	Trail Making Test (B)	125.7 (62.5)	127.5 (62.4)	12 months, all 110.5 (58.1); n=158	12 months, all 117.1 (58.9); n=141	NR	NR
	Digit–Symbol Substitution Test	34.8 (9.7)	33.7 (10.3)	38.9 (10.9); n=159	37.1 (10.9); n=141	NR	NR
	Controlled Oral Word Association Test	33.1 (12.3)	31.4 (11.3)	35.3 (12.0); n=159	33.4 (12.9); n=141	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)/ RCT	Trail making B (s)	127.1 (52.6)	101 (43.5)	4 months, all 108.7 (45.5) n=33	4 months, all 107 (54.7) n=31	NR	NR
	Digit Span Backward	5.9 (2.1)	6.8 (2.5)	6.1 (2.1) n=33	6.3 (2.2) n=31	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90) / RCT	Trail Making Test B (s)	154.2 (51.1)	156.3 (50.3)	6 months 164.0 (63.4); n=77	6 months 176.0 (57.0); n=75	NR	NR
Gold, 1995#[15] Low MAP (n=124) vs. High MAP (n=124)/ RCT	Controlled Oral Word Assoc.	37.5 (13.1)	37.6 (13.4)	change 0.0 (8.3); n=113	change 0.6 (6.1); n=112	NR	NR
	Trail Making B (s)	104.6 (60.8)	102.6 (49.3)	change -3.6 (46.9) n=113	change -13.9 (39.3) n=112	NR	NR
Andrew, 2001[21] Extracardiac (n=59) vs. Intracardiac (n=50)/ Prospective	Controlled Oral Word Association	33.5 (11.5)	34.2 (12.1)	6 months, all % with deficit 4.5; n=44	6 months, all % with deficit 0; n=30	NR	NR
	Trail making B (s)	117.0 (60.6)	129.7 (68.6)	% with deficit 18.2; n=44	% with deficit 20; n=30	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	Digital Symbol subtest, WAIS-R	36.2 (10.2)	36.0 (12.5)	% with deficit 6.8; n=44	% with deficit 26.7; n=30	NR	NR

* Decision to participate in neurocognitive testing was optional but decided prior to randomization to avoid biases.

Language Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Jensen, 2006;[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	COWAT, Number of F, A, and S words for 1 min each	30 (26-33)* n=33	25 (22-27)* n=37	6 mos. 30 (28-32)* n=30	6 mos. 29 (27-31)* n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	COWAT, # F, A, and S words for 1 min each	34.0 (11.3); n=60	36.4 (11.2); n=60	12 mos. † 36.0 (13.3); n=54	12 mos. † 38.6 (12.0); n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT	Vocabulary, WAIS-III	32.0 (13.8); n=30	38.0 (14.5); n=30	29.7 (13.4); n=27	39.9 (14.2); n=26	NR	NR
Selnes, 2009[20] CABG (off) (n=75) vs. CABG (on) (n=152)/ Prospective	Boston Naming Test	26.0 (3.7) n=71	26.2 (3.7) n=152	12 mos. ** 26.5 (3.7) n=55	12 mos. ** 27.1 (2.9) n=124	72 mos. 26.3 (3.7) n=43	72 mos. 25.9 (4.0) n=95
Selnes, 2009[20] CABG (Off) (n=75) vs. Non-surgical	Boston Naming Test	26.0 (3.7) n=71	26.1 (3.6) n=99	12 mos. ** 26.5 (3.7)	12 mos. ** 26.7 (3.3)	72 mos. 26.3 (3.7)	72 mos. 26.5 (3.0)

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
control (n=99)/ Prospective				n=55	n=91	n=43	n=67
Selnes, 2009[20] CABG (on) (n=152) vs. Non-surgical control (n=99)/ Prospective	Boston Naming Test	26.2 (3.7) n=152	26.1 (3.6) n=99	12 mos. ** 27.1 (2.9) n=124	12 mos. ** 26.7 (3.3) n=91	72 mos. 25.9 (4.0) n=95	72 mos. 26.5 (3.0) n=67
Boodhwani, 2007[6] Hypothermic (n=133) vs. Normothermic (n=134) / RCT	Letter fluency	31.7 (12.1)	32.2 (12.4)	3 months change 2.6 (7.2); n=119	3 months change 1.0 (8.1); n=117	NR	NR
	Category fluency (animal)	18.4 (4.7)	18.5 (4.9)	change 0.0 (3.9) n=119	change -0.0 (4.2) n=117	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) vs. Hypothermic (n=111)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Djaiani, 2012[9] Cell-saver (n=84) vs. Control (n=86)/ RCT	Verbal fluency	36.41 (12.57)	34.77 (10.61)	1 year, all 38.08 (12.23); n=85	1 year, all 37.02 (11.15); n=83	NR	NR
Anastasiadis, 2011[10] MECC (n=32) vs. CECC (n=32) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53) / RCT	Horn's performance test, subtest VI	61.67 (9.62)	57.82 (12.77)	3 months 61.09 (10.76); n=43	3 months 58.48 (12.94); n=44	NR	NR
	Controlled Oral Word Association Test	33.1 (12.3)	31.4 (11.3	35.3 (12.0); n=159	33.4 (12.9); n=141	NR	NR
	Semantic Fluency Test	17.7 (4.6)	17.1 (4.7)	17.4 (4.8); n=159	17.5 (5.1); n=141	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl	Controlled Oral Word Association Test	33.1 (12.3)	31.4 (11.3)	12 months, all 35.3 (12.0); n=159	12 months, all 33.4 (12.9); n=141	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
(n=180) vs. CABG with high dose fentanyl (n=170)/ RCT	Semantic Fluency Test	17.7 (4.6)	17.1 (4.7)	17.4 (4.8); n=159	17.5 (5.1); n=140	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Gold, 1995[15]# Low MAP (n=124) vs. High MAP (n=124)/ RCT	Boston Naming Test	24.6 (4.4)	24.6 (4.6)	6 months, all change 0.4 (2.0); n=113	6 months, all change 0.8 (2.3); n=112	NR	NR
	Controlled Oral Word Assoc.	37.5 (13.1)	37.6 (13.4)	change 0.0 (8.3); n=113	change 0.6 (6.1); n=112	NR	NR
Andrew, 2001[21] Extracardiac (n=59]) vs. Intracardiac (n=50)/ OBS	Boston Naming Test	54.0 (5.0)	54.7 (3.6)	6 months % with deficit 2.3; n=44	6 months % with deficit 6.7; N=30	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG
Memory Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Jensen, 2006;[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	Visual Verbal learning, cumulated recall, # words	21.9 (4.8); n=61	21.8 (5.6); n=59	12 mos., all 23.8 (4.7); n=47	12 mos., all 22.8 (4.5); n=43	NR	NR
	Visual Verbal learning, delayed recall, # words	6.7 (2.7); n=61	6.7 (2.7); n=59	7.8 (2.7); n=47	7.4 (2.5); n=43	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	Claeson-Dahl, verbal learning	151 (129-172)* n=33	174 (150-198)* n=37	6 mos., all 148 (132-165)* n=30	6 mos., all 152 (132-172)* n=32	NR	NR
	Claeson-Dahl, verbal retention	63 (55-71)* n=33	66 (59-73)* n=37	66 (61-72)* n=30	61 (55-67)* n=32	NR	NR
	Digit Symbol (WAIS-R), free recall	7.4 (6.8-7.9;)* n=33	7.1 (6.6-7.6);* n=37	7.7 (7.3-8.0);* n=30	7.6 (7.3-7.9);* n=32	NR	NR
	Digit Symbol A (WAIS-R)	5.6 (4.8-6.4);* n=33	5.0 (4.1-5.8)* n=37	5.7 (5.2-6.2);* n=30	6.0 (5.4-6.5);* n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	RAVLT -L, # words	33.6 (8.9); n=60	35.7 (7.9); n=60	12 mos., all† 37.4 (10.7); n=54	12 mos., all† 41.8 (7.9); n=52	NR	NR
	RAVLT -R, delayed recall, # words	6.0 (2.7); n=60	6.4 (2.6); n=60	7.2 (2.9); n=54	7.9 (2.6); n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT CABG (n=30)/ RCT	RAVLT, total	36.1 (13.1); n=30	39.2 (16.1); n=30	12 mos., all 42.9 (12.0); n=27	12 mos., all 43.7 (14.8); n=26	NR	NR
	RAVLT, recognition	11.7 (3.2); n=30	13.2 (1.9); n=30	13.6 (1.8); n=27	13.7 (1.5); n=26	NR	NR
	Benton Visual Retention, correct	5.5 (1.9); n=30	6.6 (2.5); n=30	5.5 (1.9); n=27	6.5 (1.9); n=26	NR	NR
	Benton Visual Retention, error	7.5 (3.3); n=30	5.5 (4.6); n=30	7.7 (3.8); n=27	5.7 (4.7); n=26	NR	NR
Selnes, 2009[20] CABG (Off) (n=75) vs. CABG (On) (n=152)/ Prospective	RAVLT, total	38.5 (9.2); n=72	39.1 (8.8); n=152	12 mos., all** 42.3 (10.3); n=55	12 mos., all** 44.6(10.6);n=124	72 mos., all 40.0 (11.2); n=43	72 mos., all 39.4 (10.4); n=96
	RAVLT, retention	69.8 (25.2); n=71	70.3(25.5);n=152	83.5 (26.1); n=55	79.6(23.7);n=124	84.5 (27.6); n=43	70.0 (26.1); n=96
	RAVLT, recognition	9.5 (4.1); n=72	9.6 (3.7); n=151	10.4 (3.2); n=55	10.7 (3.5); n=124	10.4 (3.7); n=43	9.1 (4.4); n=95
	Rey Complex Figure, delayed recall	15.4 (7.9); n=71	16.6 (7.0); n=152	20.3 (7.5); n=55	19.5 (7.4); n=123	17.7 (7.7); n=43	16.1 (7.7); n=94

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	Rey Complex Figure, retention	45.6 (21.8); n=71	50.2(19.1);n=152	60.0 (20.2); n=55	58.0(20.2);n=123	53.0 (21.0); n=43	50.4(21.5);n=94
Selnes, 2009[20] CABG (Off) (n=75) vs. Non-surgical control (n=99)/ Prospective	RAVLT, total	38.5 (9.2); n=72	41.2 (8.8); n=99	12 mos., all** 42.3 (10.3); n=55	12 mos., all** 45.5 (10.4); n=91	72 mos., all 40.0 (11.2); n=43	72 mos., all 42.9 (11.6); n=67
	RAVLT, retention	69.8 (25.2); n=71	76.6 (23.1); n=99	83.5 (26.1); n=55	80.3 (23.6); n=91	84.5 (27.6); n=43	77.8 (28.1); n=67
	RAVLT, recognition	9.5 (4.1); n=72	10.1 (3.7); n=99	10.4 (3.2); n=55	10.7 (3.9); n=91	10.4 (3.7); n=43	9.5 (5.8); n=67
	Rey Complex Figure, delayed recall	15.4 (7.9); n=71	16.4 (6.8); n=99	20.3 (7.5); n=55	18.4 (7.6); n=91	17.7 (7.7); n=43	16.7 (8.0); n=65
	Rey Complex Figure, retention	45.6 (21.8); n=71	48.8 (18.1); n=99	60.0 (20.2); n=55	54.7 (20.4); n=91	53.0 (21.0); n=43	51.2 (22.6); n=65
Selnes, 2009[20] CABG (On) (n=152) vs. Non-surgical control (n=99)/ Prospective	RAVLT, total	39.1 (8.8); n=152	41.2 (8.8); n=99	12 mos., all** 44.6(10.6);n=124	12 mos., all** 45.5 (10.4); n=91	72 mos., all 39.4 (10.4); n=96	72 mos., all 42.9 (11.6); n=67
	RAVLT, retention	70.3(25.5);n=152	76.6 (23.1); n=99	79.6(23.7);n=124	80.3 (23.6); n=91	70.0 (26.1); n=96	77.8 (28.1); n=67
	RAVLT, recognition	9.6 (3.7); n=151	10.1 (3.7); n=99	10.7 (3.5); n=124	10.7 (3.9); n=91	9.1 (4.4); n=95	9.5 (5.8); n=67
	Rey Complex Figure, delayed recall	16.6 (7.0); n=152	16.4 (6.8); n=99	19.5 (7.4); n=123	18.4 (7.6); n=91	16.1 (7.7); n=94	16.7 (8.0); n=65
	Rey Complex Figure, retention	50.2(19.1);n=152	48.8 (18.1); n=99	58.0(20.2);n=123	54.7 (20.4); n=91	50.4(21.5);n=94	51.2 (22.6); n=65
Boodhwani, 2007[6] Hypothermic (n=133) vs. Normothermic (n=134) / RCT	RAVLT: Total (T1-T5)	score 37.8 (9.2)	score 38.4 (9.6)	3 months, all change 0.3 (7.1) n=119	3 months, all change -1.0 (7.6) n=117	NR	NR
	Trial 6	score 7.2 (2.9)	score 7.2 (3.2)	change -0.1 (2.4) n=119	change -0.4 (2.6) n=117	NR	NR
	Trial 7 (delayed recall)	score 6.9 (3.1)	score 6.9 (3.2)	change -0.4 (2.5) n=119	change -0.5 (2.4) n=117	NR	NR
	Retention	score -2.5 (2.0)	score -2.6 (2.0)	change -0.5 (2.4) n=119	change -0.3 (2.7) n=117	NR	NR
	Recognition	score 12.6 (2.1)	score 12.7 (2.5)	change -0.2 (1.9) n=119	change -0.4 (2.2) n=117	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112) vs. Hypothermic (n=111)/ RCT	Buschke – free recall	41.1 (8.6), all 5-yr completers: 41.1 (8.8)	40.2 (8.8), all 5-yr completers: 41.1 (8.8)	NR	NR	5 years, all Change 0.7 (8.7) n=65	5 years, all Change 1.2 (8.5) n=66
	Buschke consistent long-term retrieval	18.4 (12), all 5-yr completers: 20.1 (2.6)	20.4 (12.7), all 5-yr completers: 20.5 (12.2)	NR	NR	Change 1.3 (12.2); n=65	Change 1.8 (12.7); n=66
	Buschke long-term retrieval	26.1 (13)), all 5-yr completers: 26.3 (12.7)	24.7 (12.5), all 5-yr completers: 26.3 (12.9	NR	NR	Change 2.2 (3.3); n=65	Change 2.5 (13.4); n=66

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	Buschke – long-term storage	29.0 (13.0), all 5-yr completers: 29.7 (12.7)	27.5 (13.0), all 5-yr completers: 28.8 (13.0)	NR	NR	Change 1.9 (4.1) n=65	Change 2.6 (14.3); n=66
	Buschke – delayed recall	6.0 (2.8), all 5-yr completers: 6.5 (2.7)	6.1 (2.8), all 5-yr completers: 6.4 (2.8)	NR	NR	Change −0.4 (2.3); n=65	Change −0.5 (2.2); n=66
Djaiani, 2012[9] Cell-saver (n=84) vs. Control (n=86)/ RCT	RAVLT	7.04 (2.88)	7.69 (2.90)	1 year, all 7.24 (3.39); n=84	1 year, all 7.36 (3.05); n=84	NR	NR
Anastasiadis, 2011[10] MECC (n=32) vs. CECC (n=32) / RCT	Fuld Object Memory Evaluation, short-term storage	43.3 (4.1); n=32	41.5 (5.2); n=32	3 mos., all 45.7 (3.8); n=29	3 mos., all 39.5 (6.4); n=31	NR	NR
	Fuld Object Memory Evaluation, long-term retrival	7.8 (1.3); n=32	7.5 (1.4); n=32	8.4 (1.3); n=29	6.5 (1.2); n=31	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53) / RCT	Wechsler memory scale, Immediate recall: memo test	6.19 (1.16)	5.55 (1.42)	6.46 (1.2); n=43	6.66 (1.3); n=44	NR	NR
	Wechsler memory scale, Delayed recall: memo test	4.60 (2.19)	3.64 (2.39)	5.63 (2.43); n=43	5.10 (2.43); n=44	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170) / RCT	Consortium to Establish a Registry for Alzheimer's Disease Auditory Verbal Learning Test	16.5 (3.7)	16.1 (4.1)	12 months 17.9 (3.7); n=159	12 months 17.2 (3.7); n=141	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)/ RCT	Adult memory and information processing, Table A	52.9 (15.8)	59 (14.6)	4 months, all 55.5 (13.7); n=31	4 months, all 61.1 (15.1); n=33	NR	NR
	RAVLT	41.2 (9.6)	37.8 (11.5)	40.6 (10.4); n=31	39.4 (11); n=33	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90) / RCT	RAVLT, Immediate recall	40.6 (6.6)	42.7 (5.6)	6 months, all 43.1 (7.7); n=77	6 months, all 45.1 (11.7); n=75	NR	NR
	RAVLT, Delayed recall	22.4 (3.9)	23.1 (3.5)	25.2 (5.4); n=77	25.6 (7.7); n=75	NR	NR
Gold, 1995[15]				6 months, all	6 months, all		

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Low MAP (n=124) vs. High MAP (n=124)/ RCT	Benton Visual Recall correct	4.9 (2.4)	5.3 (2.1)	change 0.8 (1.9); n=112	change 0.5 (1.9); n=113	NR	NR
	Benton Recognition	7.6 (1.8)	7.8 (1.7)	change 0.1 (2.0); n=112	change 0.1 (2.2); n=113	NR	NR
	Mattis-Kovner Verbal Recall	10.5 (3.4)	10.6 (3.5)	change 1.3 (3.6); n=112	change 1.1 (3.4); n=113	NR	NR
	Mattis-Kovner Recognition	2.7 (0.7)	2.7 (0.8)	change 0.11 (0.72); n=112	change 0.08 (0.79); n=113	NR	NR
Andrew, 2001[21] Extracardiac (n=59]) vs. Intracardiac (n=50)/ OBS	CA Verbal Learning Test - Total	43.0 (11.5)	40.2 (10.6)	6 months, all % with deficit, all 4.5 n=44	6 months, all % with deficit, all 6.7 n=30	NR	NR
	CA Verbal Learning Test – Short Free	8.3 (3.3)	7.6 (3.3)	9.1 n=44	20 n=30	NR	NR
	CA Verbal Learning Test - Short Cued	9.6 (2.9)	8.9 (2.8)	4.5 n=44	6.7 n=30	NR	NR
	CA Verbal Learning Test – Long Free	9.1 (3.4)	8.6 (3.1)	9.1 n=44	13.3 n=30	NR	NR
	CA Verbal Learning Test – Long Cued	9.5 (3.3)	9.1 (3.0)	0 n=44	3.3 n=30	NR	NR
	CA Verbal Learning Test – Disc.	90.2 (7.5)	90.1 (8.0)	7.0 n=44	13.3 n=30	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG
Psychomotor Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	Trail Making B (s)	158.0 (88.1); n=721*	163.7 (89.5); n=711*	30 days, change -10.9 (58.1); n=470*	30 days, change -4.7 (71.2); n=487*	1 year, change -6.8 (64.0); n=353*	1 year, change -3.2 (70.2); n=340*
Jensen, 2006;[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	Digit Symbol, 90 seconds (WAIS-R) (s)	40 (37-44-*range*) n=33	36 (33-40); n=37	6 mos., all 42 (41-44); n=30	6 mos., all 39 (36-41); n=32	NR	NR
	Trail Making A (s)	34 (30-38)	37 (31-42)	32 (29-35); n=30	34 (32-37); n=32	NR	NR
	Trail Making B (s)	82 (72-92)	104 (86-122)	84 (80-87); n=30	83 (74-92); n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	Grooved Pegboard (s)	84.5 (19.3); n=60	81.3 (16.9); n=60	12 mos., all† 78.8 (16.8); n=54	12 mos., all† 78.8 (16.1); n=52	NR	NR
	Trail Making, Part B – Part A (s)	68.3 (30.9); n=60	65.3 (41.9); n=60	63.2 (37.5); n=54	60.4 (37.4); n=52	NR	NR
	Digit Symbol (WAIS-R) (s)	36.6 (8.9); n=60	36.4 (9.6); n=60	38.5 (10.2); n=54	39.1 (10.1); n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT	Grooved Pegboard. Dominant (s)	97.8 (30.7); n=30	96.8 (46.9); n=30	12 mos., all 91.5 (26.0); n=27	12 mos., all 91.5 (26.0); n=26	NR	NR
	Grooved Pegboard. Non-dominant (s)	100.9 (124.5); n=30	97.2 (37.2); n=30	97.6 (32.2); n=27	89.6 (29.6); n=26	NR	NR
	Finger Tapping, dominant (number of taps)	37.1 (10.5); n=30	41.4 (10.0); n=30	39.4 (9.1); n=27	39.1 (10.0); n=26	NR	NR
	Digit Symbol (WAIS-III) (s)	45.3 (17.0); n=30	52.5 (17.0); n=30	43.7 (14.5); n=27	53.8 (22.1); n=26	NR	NR
	Trail Making A (s)	47.4 (22.2); n=30	43.7 (32.6); n=30	45.7 (15.2); n=27	43.4 (34.4); n=26	NR	NR
	Trail Making B (s)	126.0 (86.7);n=30	114.9 (87.6); n=30	117.3 (63.4); n=27	104.4 (92.1); n=26	NR	NR
Selnes, 2009[20] CABG (Off) (n=75) vs. CABG (on) (n=152)/ Prospective	Grooved Pegboard. Dominant (s)	99.6 (30.9) n=67	107.5 (53.7); n=152	12 mos., all** 94.2 (32.1) n=54	12 mos., all** 95.6 (29.9) n=122	72 mos., all 96.0 (34.4) n=43	72 mos., all 105.5 (36.0); n=93
	Grooved Pegboard. Non-dominant (s)	107.0 (34.4) n=68	119.1 (65.3); n=149	98.1 (30.3); n=54	103.4 (30.6); n=123	99.0 (30.4) n=43	116.3 (41.3); n=94

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	Trail Making A (s)	48.0 (23.0) n=69	47.1 (24.2); n=151	43.4 (17.5); n=55	40.8 (16.8); n=123	42.6 (15.9) n=43	47.7 (29.5); n=95
	Trail Making B (s)	96.9 (34.7); n=68	105.2 (59.0); n=147	97.2 (48.4); n=55	95.4 (48.2); n=122	101.1 (47.1); n=43	105.0 (50.1); n=91
Selnes, 2009[20] CABG (Off) (n=75) vs. Non-surgical control (n=99)/ Prospective	Grooved Pegboard. Dominant (s)	99.6 (30.9); n=67	97.9 (29.7); n=99	12 mos., all** 94.2 (32.1); n=54	12 mos., all** 90.8 (24.6); n=91	72 mos., all 96.0 (34.4); n=43	72 mos., all 103.3 (42.0)n=67
	Grooved Pegboard. Non-dominant (s)	107.0 (34.4) n=68	107.4 (38.4) n=98	98.1 (30.3) n=54	102.5 (35.6); n=89	99.0 (30.4) n=43	111.6 (42.9) n=66
	Trail Making A (s)	48.0 (23.0); n=69	43.1 (14.4); n=99	43.4 (17.5); n=55	41.0 (15.6); n=91	42.6 (15.9); n=43	46.4 (31.6); n=66
	Trail Making B (s)	96.9 (34.7); n=68	95.4 (40.0); n=99	97.2 (48.4); n=55	92.0 (41.5); n=91	101.1 (47.1)n=43	100.4 (50.6)n=66
Selnes, 2009[20] CABG (On) (n=152) vs. Non-surgical control (n=99)/ Prospective	Grooved Pegboard. Dominant (s)	107.5 (53.7); n=152	97.9 (29.7) n=99	12 mos., all** 95.6 (29.9) n=122	12 mos., all** 90.8 (24.6); n=91	72 mos., all 105.5 (36.0); n=93	72 mos., all 103.3 (42.0) n=67
	Grooved Pegboard. Non-dominant (s)	119.1 (65.3); n=149	107.4 (38.4) n=98	103.4 (30.6) n=123	102.5 (35.6); n=89	116.3 (41.3); n=94	111.6 (42.9) n=67
	Trail Making A (s)	47.1 (24.2); n=151	43.1 (14.4) n=99	40.8 (16.8); n=123	41.0 (15.6); n=91	47.7 (29.5); n=95	46.4 (31.6) n=66
	Trail Making B (s)	105.2 (59.0); n=147	95.4 (40.0) n=99	95.4 (48.2) n=122	92.0 (41.5) n=91	105.0 (50.1); n=91	100.4 (50.6) n=66
Boodhwani, 2007[6] Hypothermic (n=133) vs. Normothermic (n=134) / RCT	Trail Making A (s)	41.9 (14.8)	40.2 (12.3)	3 months, all -4.0 (12.3) n=119	3 months, all -1.4 (11.9) n=117	NR	NR
	Trail making B (s)	105.6 (45.0)	103.3 (43.3)	-11.7 (29.0) n=119	-7.8 (35.5) n=117	NR	NR
	Grooved pegboard, dominant (s)	90.1 (20.5)	91.1 (24.4)	-4.0 (13.4) n=119	-2.0 (14.8) n=117	NR	NR
	Grooved pegboard, nondominant (s)	99.2 (26.6)	100.1 (28.3)	-4.3 (18.2) n=119	-3.5 (13.7) n=117	NR	NR
	Symbol Digit Modalities Test	42.9 (9.4)	43.1 (9.7)	2.1 (5.3) n=119	1.8 (6.7) n=117	NR	NR
	Finger tapping (dominant)	46.9 (7.9)	46.8 (8.1)	1.3 (4.9) n=119	1.6 (5.8) n=117	NR	NR
	Finger tapping (nondominant)	43.9 (7.4)	43.6 (7.3)	0.6 (3.7) n=119	1.2 (5.3) n=117	NR	NR
Nathan, 2001;[7] 2007[8] Normothermic (n=112] vs. Hypothermic (n=111)/ RCT	Trail making A (s)	39.8 (12.3), all 5-yr completers: 38.7 (11.5)	39.4 (12.0), all 5-yr completers: 39.9 (11.6)	NR	NR	5-years, all Change 6.5 (19.0); n=65	5-years, all Change 2.9 (1.8); n=66
	Grooved pegboard (s)	89.0 (19.5), all 5-yr completers: 88.2 (17.0)	87.5 (19.6), all 5-yr completers: 87.5 (20.7)	NR	NR	Change 14.7 (30.7); n=65	Change 13.7 (21.6); n=66
	Symbol Digit	42.1 (11.0), all 5-yr completers:	43.1 (10.1), all 5-yr completers:	NR	NR	Change −3.4 (6.8); n=65	Change −2.9 (5.8); n=66

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	Modalities Test	42.8 ± 11.1	43.8 ± 10.6				
Djaiani, 2012[9] Cell-saver (n=84) vs. Control (n=86)/ RCT	Grooved Pegboard (s)	89.97 (18.68)	91.32 (21.85)	1 year, all 89.1 (18.8) n=84	1 year, all 86.1 (23.4) n=83	NR	NR
Anastasiadis, 2011[10] MECC vs. CECC / RCT	Digit Symbol Modalities Test	36.7 (15.9); n=32	29.7 (17.2); n=32	3 mos. 43.2 (17.1); n=29	3 mos. 24.2 (17.7); n=31	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs control: CABG with placebo (n=53) / RCT	Trail making A (s)	43.2 (10.9)	42.6 (10.7)	3 months, all 44.1 (14.5) n=43	3 months, all 47.2 (10.1) n=44	NR	NR
	Trail making B (s)	40.53 (10.1)	40.7 (10.9)	44.8 (11.3); n=43	45.5 (12.8); n=44	NR	NR
	Zimmermann and Fimm Change of reaction, median reaction time	37.95 (10.66)	38.25 (12.69)	44.10 (12.47); n=43	43.90 (14.16); n=44	NR	NR
	Zimmermann and Fimm Change of reaction, SD of reaction time	42.26 (13.99)	45.77 (17.82)	53.13 (18.90); n=43	53.55 (19.72); n=44	NR	NR
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170) / RCT	Trail Making A (s)	55.0 (25.7)	54.6 (23.6)	12 months, all 48.0 (18.1); n=159	12 months, all 50.8 (22.6); n=140	NR	NR
	Trail Making B (s)	125.7 (62.5)	127.5 (62.4)	110.5 (58.1); n=158	117.1 (58.9); n=141	NR	NR
	Grooved Pegboard Test, dominant (s)	99.7 (30.6)	102.1 (34.5)	90.6 (30.7); n=155	91.6 (28.0); n=138	NR	NR
	Grooved Pegboard Test, nondominant (s)	110.2 (39.2)	108.5 (37.8)	100.1 (34.3); n=155	98.6 (22.3); n=136	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33)/ RCT	Trail making A (s)	41.7 (14.9)	43 (16.3)	4 months, all 40.6 (15.7) n=31	4 months, all 41.4 (15.5) n=33	NR	NR
	Trail making B (s)	101 (43.5)	127.1 (52.6)	107 (54.7) n=31	108.7 (45.5)n=33	NR	NR
	Grooved Pegboard, dominant (s)	19.1 (2.2)	19.7 (2.8)	19.1 (2.6) n=31	19.1 (2.5) n=33	NR	NR
	Grooved Pegboard, nondominant (s)	21 (2.3)	21.1 (3)	20.4 (2.6) n=31	20.9 (3.7) n=33	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90) / RCT	Trail Making A (s)	42.5 (6.6)	43.2 (5.6)	6 months, all 44.1 (5.7); n=77	6 months, all 45.4 (6.9); n=75	NR	NR
	Trail Making B (s)	154.2 (51.1)	156.3 (50.3)	164.0 (63.4); n=77	176.0 (57.0); n=75	NR	NR
	Grooved pegboard (s)	21.9 (3.0)	22.0 (3.5)	23.2 (4.0); n=77	23.2 (4.3); n=75	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Gold, 1995[15] Low MAP (n=124) vs. High MAP (n=124)/ RCT	Trail Making A (s)	43.7 (22.3)	45.2 (24.7)	6 months, all change -2.7 (15.4) n=113	6 months, all change -4.0 (20.3) n=112	NR	NR
	Trail Making B (s)	104.6 (60.8)	102.6 (49.3)	change -3.6 (46.9) n=113	change -13.9 (39.3) n=112	NR	NR
	Digit Symbol	41.4 (10.7)	40.9 (13.7)	change 3.7 (6.7) n=112	change 2.5 (5.9) n=113	NR	NR
	Digit Span	14.2 (4.0)	14.8 (3.9)	change 0.4 (2.9) n=112	change 0.0 (3.1) n=113	NR	NR
	Finger Tapping (dominant)	46.2 (10.1)	46.6 (10.3)	change 0.9 (7.0) n=112	change -1.4 (9.3) n=113	NR	NR
Andrew, 2001[21] Extracardiac (n=59]) vs. Intracardiac (n=50)/ OBS	Purdue Pegboard (Right)	11.1 (2.2)	11.4 (2.3)	6 months, all % with deficit, all 2.3; n=44	6 months, all % with deficit, all 0; n=30	NR	NR
	Purdue Pegboard (Left)	10.8 (2.1)	10.8 (2.1)	7.0; n=44	0; n=30	NR	NR
	Purdue Pegboard (Right/Left)	9.0 (1.9)	8.5 (2.0)	4.7; n=44	3.3; n=30	NR	NR

* Decision to participate in neurocognitive testing was optional but decided prior to randomization to avoid biases.

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG
Visuospatial Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Lamy, 2013[1] Off-pump CABG (n=2375) vs. On-pump CABG (n=2377)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Jensen, 2006,[24] 2008[2] CABG (Off) (n=61) vs. CABG (on) (n=59)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Vedin, 2006[3] CABG (off) (n=33) vs. CABG (on) (n=37)/ RCT	Block Span (WAIS-R), forward	7.2 (6.6-7.8)* n=33	6.9 (6.3-7.6)* n=37	6 mos., all 7.1 (6.6-7.7)* n=30	6 mos. 6.4 (5.9-7.0)* n=32	NR	NR
	Block Span (WAIS-R), backward	6.6 (6.1-7.1)* n=33	5.9 (5.2-6.5)* n=37	6.2 (5.6-6.7)* n=30	5.9 (5.5-6.3)* n=32	NR	NR
Lund, 2005[4] CABG (off) (n=60) vs. CABG (on) (n=60)/ RCT	Block Design (WAIS-R)	26.4 (8.5) n=60	26.7 (9.2) n=60	12 mos. † 27.4 (9.7) n=54	12 mos. † 27.8 (9.6) n=52	NR	NR
Lee, 2003[5] CABG (off) (n=30) vs. CABG (on) (n=30)/ RCT	Benton Visual Retention, correct	5.5 (1.9); n=30	6.6 (2.5); n=30	12 mos., all 5.5 (1.9); n=27	12 mos., all 6.5 (1.9); n=26	NR	NR
	Benton Visual Retention, error	7.5 (3.3); n=30	5.5 (4.6); n=30	7.7 (3.8); n=27	5.7 (4.7); n=26	NR	NR
Selnes, 2009[20] CABG (Off) (n=75) vs. CABG (On) (n=152)/ Prospective	Rey Complex Figure, copy	32.6 (4.0); n=71	32.5 (4.7); n=152	12 mos., all** 33.4 (3.4); n=55	33.1 (3.6); n=124	72 mos., all 32.5 (3.9); n=43	31.4 (5.2); n=94
	Rey Complex Figure, delayed recall	15.4 (7.9); n=71	16.6 (7.0); n=152	20.3 (7.5); n=55	19.5 (7.4); n=123	17.7 (7.7); n=43	16.1 (7.7); n=94
	Rey Complex Figure, retention	45.6 (21.8); n=71	50.2(19.1);n=152	60.0 (20.2); n=55	58.0(20.2);n=123	53.0 (21.0); n=43	50.4(21.5);n=94
	Block design (WAIS-R)	22.9 (9.2); n=69	23.2(10.0);n=150	26.0 (9.6); n=54	26.2(10.2);n=123	25.0 (10.3); n=43	23.3 (10.2);n=93
Selnes, 2009[20] CABG (Off) (n=75) vs. Non-surgical control (n=99)/ Prospective	Rey Complex Figure, copy	32.6 (4.0); n=71	33.0 (3.2); n=99	12 mos., all** 33.4 (3.4); n=55	12 mos., all** 33.0 (3.4); n=91	72 mos., all 32.5 (3.9); n=43	72 mos., all 32.4 (3.4); n=65
	Rey Complex Figure, delayed recall	15.4 (7.9); n=71	16.4 (6.8); n=99	20.3 (7.5); n=55	18.4 (7.6); n=91	17.7 (7.7); n=43	16.7 (8.0); n=65
	Rey Complex Figure, retention	45.6 (21.8); n=71	48.8 (18.1); n=99	60.0 (20.2); n=55	54.7 (20.4); n=91	53.0 (21.0); n=43	51.2 (22.6); n=65
	Block design (WAIS-	22.9 (9.2); n=69	23.2 (9.5); n=99	26.0 (9.6); n=54	24.2 (9.6); n=91	25.0 (10.3); n=43	23.3 (9.8); n=66

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
	R)						
Selnes, 2009[20] CABG (On) (n=152) vs. Non-surgical control (n=99)/ Prospective	Rey Complex Figure, copy	32.5 (4.7); n=152	33.0 (3.2); n=99	12 mos., all** 33.1 (3.6); n=124	12 mos., all** 33.0 (3.4); n=91	72 mos., all 31.4 (5.2); n=94	72 mos., all 32.4 (3.4); n=65
	Rey Complex Figure, delayed recall	16.6 (7.0); n=152	16.4 (6.8); n=99	19.5 (7.4); n=123	18.4 (7.6); n=91	16.1 (7.7); n=94	16.7 (8.0); n=65
	Rey Complex Figure, retention	50.2(19.1);n=152	48.8 (18.1); n=99	58.0(20.2);n=123	54.7 (20.4); n=91	50.4(21.5);n=94	51.2 (22.6); n=65
	Block design (WAIS-R)	23.2(10.0);n=150	23.2 (9.5); n=99	26.2(10.2);n=123	24.2 (9.6); n=91	23.3 (10.2);n=93	23.3 (9.8); n=66
Boodhwani, 2007[6] (hypothermic [n=133 versus normothermic [n=134]]) RCT	No tests reported	NR	NR	NR	NR	NR	NR
Nathan, 2001;[7] 2007[8] (normothermic [n=112] versus hypothermic [n=111]) RCT	No tests reported	NR	NR	NR	NR	NR	NR
Djaiani, 2012[9] (cell-saver [n=84] versus control [n=86]) RCT	Spatial Span Backward	7.02 (1.62)	7.02 (1.49)	6.89 (1.85) N=84	6.87 (1.46) N=86	NR	NR
	Spatial Span Forward	7.25 (1.75)	7.27 (1.31)	7.29 (1.66); n=84	7.08 (1.37); n=86	NR	NR
Anastasiadis 2011[10] MECC (n=32) vs. CECC (n=32) / RCT	Judgment of Line Orientation	6.5 (2.8); n=32	5.3 (2.8); n=32	3 mos., all 7.24 (2.3); n=29	3 mos., all 4.9 (2.4); n=31	NR	NR
Flesch, 2009[11] CABG with candesartan (n=53) vs. CABG with placebo (n=53)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR

Appendix J. Table 1. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - CABG

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Silbert, 2006[12] CABG with low dose fentanyl (n=180) vs. CABG with high dose fentanyl (n=170) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Alex, 2005[13] Atmospheric air (n=31) vs. Hyperbaric oxygen (n=33) RCT	No tests reported	NR	NR	NR	NR	NR	NR
Kadoi, 2003[27] CABG with propofol (n=90) vs. CABG with fentanyl (n=90) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Gold, 1995[15]# Low MAP (n=124) vs.High MAP (n=124)/ RCT	Benton Visual Recall correct	4.9 (2.4)	5.3 (2.1)	6 months change 0.8 (1.9) n=112	6 months change 0.5 (1.9) n=113	NR	NR
Andrew, 2001[21] Extracardiac (n=59) vs. Intracardiac (n=50)/ OBS	No tests reported	NR	NR	NR	NR	NR	NR

CECC= conventional extracorporeal circulation; COWAT = Controlled Oral Word Association Test; MECC=minimal extracorporeal circulation; Off = off-pump; On = on-pump; NR = not reported; s = seconds; MMSE = Mini–mental state examination;mos=months; NR = not reported; s = seconds; RAVLT = Rey Auditory Verbal Learning Test; WAIS = Wechsler Adult Intelligence Scale

* Vedin: presented as 95% confidence intervals
† Lund also reported data for 3 months
§ Nathan 2001, 2007 – reported pre-procedure raw score and postoperative change.
¶ Silbert 2006 also reported data for 3 months
** Selnes 2009 (McKhann 2005) also reported data for 3 months

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Attention Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)*/ OBS	Trail Making A (s)	*z scores (mean ± SD) transformed from raw scores* −0.197 (0.999)	NR	*z scores (mean ± SD) transformed from raw scores* −0.292 (1.031)	NR	NR	NR
	Digit span forward	−0.003 (1.000)	NR	0.367 (0.932)	*z-score difference from baseline (from graph)* ~ -0.25		
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	Trail Making A (s)	44.5 (17.3)	40.8 (15.7)	6 months % with deficit 33.3 n=30	6 months % with deficit 25.0 n=44	NR	NR

NR = not reported** Mini-Mental State Exam also reported. ""In the MMSE and digit span backward test, a non-significant decline at discharge (z-score difference, −0.72 ± 1.42 and −0.20 ± 1.15, respectively) was followed by a significant increase by 3 months (z-score difference 0.95 ± 1.20 and 0.98 ± 1.45, respectively, P <0.05)."

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Executive Function Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)/ OBS	Trail Making B (s)	*z scores (mean ± SD) transformed from raw scores* −0.232 (0.999)	NR	*z scores (mean ± SD) transformed from raw scores* −0.342 (0.757)	NR	NR	NR
	Digit span backward	0.003 (1.001)	NR	0.015 (0.888)	*z-score difference from baseline (from graph)* ~ 0.67		
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	Controlled Oral Word Association	34.2 (12.1)	33.5 (11.5)	6 months, all % with deficit, 0; n=30	6 months, all % with deficit 4.5; n=44	NR	NR
	Trail making B (s)	129.7 (68.6)	117.0 (60.6)	% with deficit 20; n=30	% with deficit 18.2; n=44	NR	NR
	Digital Symbol	36.0 (12.5)	36.2 (10.2)	% with deficit 26.7; n=30	% with deficit 6.8; n=44	NR	NR

NR = not reported

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Language Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)/ OBS	Verbal fluency	NR	NR	NR	*z-score difference from baseline (from graph) ~ -0.25*	NR	NR
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30)/ RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	Controlled Oral Word Association	34.2 (12.1)	33.5 (11.5)	6 months, all % with deficit, all 0 n=30	6 months, all % with deficit, all 4.5 n=44	NR	NR
	Boston Naming Test	54.7 (3.6)	54.0 (5.0)	6 months % with deficit 6.7 n=30	6 months % with deficit 2.3 n=44	NR	NR

NR = not reported

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Memory Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)/ OBS	Verbal Learning Test - immediate recall	−0.004 (0.998)	NR	*z scores (mean ± SD) transformed from raw scores* 0.005 (0.839)	*z-score difference from baseline (from graph) ~0.4*	NR	NR
	Verbal Learning Test - delayed recognition	0.211 (0.998)	NR	*z scores (mean ± SD) transformed from raw scores* 0.469 (1.002)	*z-score difference from baseline (from graph) ~0.15*	NR	NR
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30) / RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	CA Verbal Learning Test - Total	40.2 (10.6)	43.0 (11.5)	6 months, all % with deficit 6.7; n=30	6 months, all % with deficit 4.5; n=44	NR	NR
	CA Verbal Learning Test – Short Free	7.6 (3.3)	8.3 (3.3)	% with deficit 20; n=30	% with deficit 9.1; n=44	NR	NR
	CA Verbal Learning Test - Short Cued	8.9 (2.8)	9.6 (2.9)	% with deficit 6.7; n=30	% with deficit 4.5; n=44	NR	NR
	CA Verbal Learning Test – Long Free	8.6 (3.1)	9.1 (3.4)	% with deficit 13.3; n=30	% with deficit 9.1; n=44	NR	NR
	CA Verbal Learning Test – Long Cued	9.1 (3.0)	9.5 (3.3)	% with deficit 3.3; n=30	% with deficit 0; n=44	NR	NR
	CA Verbal Learning Test – Disc.	90.1 (8.0)	90.2 (7.5)	% with deficit 13.3; n=30	% with deficit 7.0; n=44	NR	NR

NR = not reported

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Psychomotor Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knipp, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)/ OBS	Trail Making A (s)	*z scores (mean ± SD) transformed from raw scores* −0.197 (0.999)	NR	*z scores (mean ± SD) transformed from raw scores* −0.292 (1.031)	NR	NR	NR
	Trail Making B (s)	*z scores (mean ± SD) transformed from raw scores* −0.232 (0.999)	NR	*z scores (mean ± SD) transformed from raw scores* −0.342 (0.757)	NR	NR	NR
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30) /RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	Trail Making A (s)	44.5 (17.3)	40.8 (15.7)	6 months % with deficit 33.3; n=30	6 months % with deficit 25.0; n=44		
	Trail making B (s)	129.7 (68.6)	117.0 (60.6)	6 months % with deficit 20; n=30	6 months % with deficit 18.2; n=44	NR	NR
	Pegboard (Right)	11.4 (2.3)	11.1 (2.2)	6 months % with deficit 0; n=30	6 months % with deficit 2.3; n=44	NR	NR
	Pegboard (Left)	score 10.8 (2.1)	score 10.8 (2.1)	6 months % with deficit 0; n=30	6 months % with deficit 7.0; n=44	NR	NR
	Pegboard (Right/Left)	score 8.5 (2.0)	score 9.0 (1.9)	6 months % with deficit 3.3; n=30	6 months % with deficit 4.7; n=44	NR	NR

NR = not reported

Appendix J. Table 2. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains - AVR
Visual/Spatial Domain

Study	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Knip, 2013[23] AVR (n=37) Transapical transcatheter aortic valve implantation (n=27)/ OBS	Corsi block tapping forward	*z scores (mean ± SD) transformed from raw scores* 0.003 (0.999)	NR	*z scores (mean ± SD) transformed from raw scores* 0.073 (1.122)	NR	NR	NR
	Corsi block tapping backward	0.002 (1.002)	NR	0.164 (1.023)	NR	NR	NR
	Horn test No. 9	−0.001 (0.999)	NR	0.324 (1.055)	NR	NR	NR
Fakin, 2012[18] Hypothermic AVR (n=30) vs. Normothermic (n=30)/RCT	No tests reported	NR	NR	NR	NR	NR	NR
Andrew, 2001[21] Intracardiac (n=50) vs. Extracardiac (n=59)/ OBS	No tests reported	NR	NR	NR	NR	NR	NR

NR = not reported

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Attention Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69)/ RCT	WAIS-III Digit Span Forward, z-score	0.91 (1.26)	0.50 (0.69)	6 months, all change: −0.09 (1.05); n=61	6 months, all change: −0.13 (1.60); n=58	NR	NR
	Star cancellation of the behavioral inattention task, z-score	1.18 (1.79)	0.44 (3.56)	change: −1.75 (1.70); n=61	change: −0.61 (3.57); n=58	NR	NR
Baracchini 2012 CEA (n=145) vs. Laparoscopic cholecystectomy control (n=68) / OBS	No tests reported	NR	NR	NR	NR	NR	NR
Crawley 2000 Carotid PTA (n=20) vs. CEA (n=26) / RCT	Trail-Making Test A (s)	47.0 (17.0)	68.8 (57.4)	6 months, all 46.3 (19.5); n=18 change: 0.05;	6 months, all 88.3 (119.4); n=22 change: 0.03	NR	NR
	Letter Cancellation Test, (s)	106.7 (25.1)	121.74 (31.7)	108.8 (23.8); n=18 change: −0.08	118.7 (29.6); n=22 change: 0.15	NR	NR
	Symbol Digit Test (s)	231.8 (66.2)	261.0 (110.2)	220.4 (65.8); n=18 change: 0.05	245.4 (107.7); n=22 change: 0.15	NR	NR
	Two-Choice Reaction Time (ms)	715.6 (241.7)	694.8 (234.9)	715.6 (232.0); n=18 change: 0.19	704.6 (205.0); n=22 change: −0.08	NR	NR
	Displaced Reaction Time (s)	1.5 (0.8)	1.6 (0.7)	1.5 (0.9); n=18 change: −0.03	1.6 (0.9); n=22 change: 0.16	NR	NR

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Executive Function Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Preoperative, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69)/ RCT	Raven advanced progressive matrices; WAIS similarities, z-score	−0.26 (0.75)	−0.49 (0.90)	6 months, all change: −0.17 (0.48); n=61	6 months, all change: 0.04 (0.45); n=58	NR	NR
	Brixton anticipation task and Letter fluency, z-score	−0.41 (0.59)	−0.61 (0.69)	change: 0.13 (0.36); n=61	change: 0.17 (0.48); n=58	NR	NR
	WAIS-III digit span backward, Rey auditory verbal learning test and Semantic fluency, z-score	0.11 (1.08)	−0.34 (1.02)	change: −0.16 (0.76); n=61	change: −0.09 (1.00); n=58	NR	NR
	Benton judgment of line orientation, Facial recognition task, and Rey-Osterrieth complex figure-copy, z-score	−0.35 (0.90)	−0.47 (0.98)	change: −0.14 (0.54)	change: −0.17 (0.73); n=58	NR	NR
Baracchini, 2012[22] CEA (n=145:) vs. laparoscopic cholecystectomy control (n=68) / OBS	No tests reported	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26) / RCT	Trail-Making Test B (s)	129.5 (76.8)	144.04 (49.2)	6 months, all 152.9 (113.7); n=18 change: −16	6 months, all 147.0 (70.6); n=22 change: 0.17	NR	NR
	Symbol Digit Test (s)	231.8 (66.2)	261.0 (110.2)	220.4 (65.8); n=18 change: 0.05	245.4 (107.7); n=22 change: 0.15	NR	NR

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Language Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69) / RCT	Token test and Boston naming test, z-score	−0.39 (0.83)	−0.61 (1.20)	6 months, all change: −0.25 (0.68); n=61	6 months, all change: −0.18 (0.70); n=58	NR	NR
	Brixton anticipation task and Letter fluency, z-score	−0.41 (0.59)	−0.61 (0.69)	change: 0.13 (0.36); n=61	change: 0.17 (0.48); n=58	NR	NR
	WAIS-III digit span backward and Rey auditory verbal learning test; semantic fluency, z-score	0.11 (1.08)	−0.34 (1.02)	change: −0.16 (0.76); n=61	change: −0.09 (1.00); n=58	NR	NR
Baracchini, 2012[22] CEA (n=145: 75 asx + 70 sx)) vs. laparoscopic cholecystectomy control (n=68) Prospective observational cohort study	No tests reported	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26) / RCT	No tests reported	NR	NR	NR	NR	NR	NR

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Memory Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69) RCT	WAIS-III digit span backward,Rey auditory verbal learning test and Semantic fluency, z-score	0.11 (1.08)	−0.34 (1.02)	6 months, all change: −0.16 (0.76); n=61	6 months, all change: −0.09 (1.00); n=58	NR	NR
	Rey-Osterrieth complex figure-delay, z-score	−0.15 (1.08)	−0.23 (0.85)	change: 0.24 (0.72); n=61	change: 0.24 (0.66); n=58	NR	NR
	Benton judgment of line orientation, Facial recognition task and Rey-Osterrieth complex figure-copy, z-score	−0.35 (0.90)	−0.47 (0.98)	change: −0.14 (0.54); n=61	change: −0.17 (0.73); n=58	NR	NR
Baracchini, 2012[22] CEA (n=145: 75 asx + 70 sx)) vs. laparoscopic cholecystectomy control (n=68) Prospective observational cohort study	No tests reported	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26) RCT	Rey Auditory Verbal Learning Test (sum of # of correct trials)	53.2 (12.3)	53.9 (12.8)	6 months, all 53.9 (16.8); n=18 change: 0.04	6 months, all 55.8 (14.9); n=22 change:0.08	NR	NR
	Nonverbal Memory Test (number correct)	16.6 (1.7)	16.7 (2.0)	16.6 (1.8); n=18 change: −0.01	16.9 (1.8); n=22 change:0.16	NR	NR

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Psychomotor Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69) RCT	No tests reported	NR	NR	NR	NR	NR	NR
Baracchini, 2012[22] CEA (n=145: 75 asx + 70 sx) vs. laparoscopic cholecystectomy control (n=68) Prospective observational cohort study	No tests reported	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26) RCT	Trail-Making Test A (s)	47.0 (17.0)	68.8 (57.4)	6 months, all 46.3 (19.5); n=18 change: 0.05	6 months, all 88.3 (119.4); n=22 change: 0.03	NR	NR
	Trail-Making Test B (s)	129.5 (76.8)	144.04 (49.2)	152.9 (113.7); n=18 change: −16	147.0 (70.6); n=22 change: 0.17	NR	NR
	Symbol Digit Test (s)	231.8 (66.2)	261.0 (110.2)	220.4 (65.8); n=18 change: 0.05	245.4 (107.7); n=22 change: 0.15	NR	NR
	Grooved Pegboard Dominant (s)	89.3 (21.8)	106.6 (33.6)	103.8 (34.3); n=18 change: −0.06	raw: 108.8 (39.6); n=22 change: 0.45	NR	NR
	Grooved Pegboard Nondominant, (s)	109.4 (32.2)	113.3 (26.3)	120.4 (47.8); n=18 change: 0.07	: 126.5 (65.7); n=22 change: 0.25	NR	NR
	Finger Tapping (number of taps)	56.7 (15.2)	50.05 (12.28)	55.8 (18.7); n=18 change: 0.20	50.8 (13.72); n=22 change: 0.12	NR	NR

Appendix J. Table 3. Cognitive Outcomes Tables: Individual Neuropsychological Tests/Cognitive Domains – CAS and CEA
Visual/Spatial Domain

Study/ Intervention vs. control / Design	Specific cognitive test	Pre-Procedure, mean (SD)		Intermediate-term, mean (SD) (3-12 months) follow-up		Long-term, mean (SD) (>12 months) follow-up	
		Intervention	Control	Intervention	Control	Intervention	Control
Altinbas, 2011[16] CAS (n=71) vs. CEA (n=69) / RCT	Rey-Osterrieth complex figure-delay, z-score	−0.15 (1.08)	−0.23 (0.85)	6 months, all change: 0.24 (0.72); n=61	6 months, allchange: 0.24 (0.66); n=58	NR	NR
	Benton judgment of line orientation, facial recognition task, Rey-Osterrieth complex figure-copy, z-score	−0.35 (0.90)	−0.47 (0.98)	change: −0.14 (0.54); n=61	change: −0.17 (0.73); n=58	NR	NR
	Star cancellation of the behavioral inattention task, z-score	1.18 (1.79)	0.44 (3.56)	change: −1.75 (1.70); n=61	change: −0.61 (3.57); n=58	NR	NR
Baracchini, 2012[22] CEA (n=145: 75 asx + 70 sx)) vs. laparoscopic cholecystectomy control (n=68) Prospective observational cohort study	No tests reported	NR	NR	NR	NR	NR	NR
Crawley, 2000[17] Carotid PTA (n=20) vs. CEA (n=26) / RCT	Letter Cancellation Test (s)	106.7 (25.1)	121.74 (31.7)	6 months 108.8 (23.8); n=18 change: −0.08	6 months 118.7 (29.6); n=22 change: 0.15	NR	NR

CEA=carotid endarterectomy; ms = milliseconds; NR = not reported; PTA = percutaneous transluminal angioplasty; s = seconds; sr=square root

Appendix K

Stroke/TIA Outcomes Tables

Appendix K. Table 1. Stroke / TIA Outcomes - CABG

Study/Design	Stroke n/N (%)		TIA n/N (%)	
	Intervention	**Control**	**Intervention**	**Control**
Lamy, 2013[1] RCT	Off-pump CABG 36/2375 (1.5); 1 year	CABG 40/2377 (1.7); 1 year	Off-pump CABG NR	CABG NR
Jensen, 2006;[24] 2008[2] RCT	Off-pump CABG 1/61 (1.6); 3 mos.	CABG 1/59 (1.7); 3 mos.	Off-pump CABG NR	CABG NR
Vedin, 2006[3] RCT	Off-pump CABG 0/33	CABG 0/37	Off-pump CABG 0/33	CABG 0/37
Lund, 2005[4] RCT	Off-pump CABG NR	CABG NR	Off-pump CABG NR	CABG NR
Lee, 2003[5] RCT	Off-pump CABG 0/30	CABG 1/30 (3.3) *Detected by scan*	Off-pump CABG NR	CABG NR
Boodhwani, 2007[6] RCT	NR	NR	NR	NR
McKhann, 2005;[28] Selnes 2009[20] Prospective	Off-pump CABG NR at 3 and 12 mos.; *4% at 72 mos.*	Non-surgical control NR at 3 and 12 mos.; *3% at 72 mos.*	Off-pump CABG NR at 3 and 12 mos. *3% at 72 mos.*	Non-surgical control NR at 3 and 12 mos. *4% at 72 mos.*
Nathan, 2001;[7] 2007[8] RCT	NR	NR	NR	NR
Djaiani, 2012[9] RCT	NR	NR	NR	NR
Anastasiadis, 2011[10] RCT	MECC 0/32	CECC 0/32	MECC 0/32	CECC 0/32
Flesch, 2009[11] RCT	Candesartan 2/43 (4.7%)	Placebo 5/44 (11.4%)	NR	NR
Silbet, 2006[12] RCT	2 post-procedure strokes (NR by group)		NR	NR
Alex, 2005[13] RCT	NR	NR	NR	NR
Kadoi, 2003[27] RCT	Propofol 3/90 (3.3%)	Fentanyl (3/90) (3.3%)	NR	NR
Gold, 1995[15] RCT	NR	NR	NR	NR
Andrew, 2001[21] Prospective	NR	NR	NR	NR

CABG = coronary artery bypass grafting; NR = not reported; TIA = transient ischemic attack; MECC = minimal extracorporeal circulation; CECC = conventional extracorporeal circulation

Appendix K. Table 2. Stroke/TIA Outcomes Tables - AVR

	Stroke		TIA	
Study	**Intervention**	**Control**	**Intervention**	**Control**
Knipp, 2013[23]	AVR 1/37 (2.7)	TA-TAVI 1 (fatal) /27 (3.7)	NR	NR
Fakin, 2012[18]	0 (0)	0 (0)	NR	NR
Andrew, 2001[21]	NR	NR	NR	NR

CABG = coronary artery bypass grafting; NR = not reported; TIA = transient ischemic attack; TA-TAVI = transapical transcatheter aortic valve implantation

Appendix K. Table 3. Stroke/TIA Outcomes Tables – CAS and CEA

	Stroke		TIA	
Study	**Intervention**	**Control**	**Intervention**	**Control**
Altinbas, 2011[16] CAS (n=71) vs CEA (n=69) RCT	6 months: There were no significant differences between CAS and CEA in the 6-month stroke rate (data were not shown).		NR	NR
Baracchini, 2012[22] Prospective observational cohort study	30 days: Symptomatic 0/75 (0)	30 days: Asymptomatic 0/70 (0)	30 days: Symptomatic3/75 (4%)	At 30 days: Asymptomatic 0/70 (0)
Crawley, 2000[17] Carotid PTA (n=20) vs CEA (n=26) RCT	NR	NR	NR	NR

asx=asymptomatic; CABG = coronary artery bypass grafting; NR = not reported; RCT=randomized controlled trial; TIA = transient ischemic attackasx=asymptomatic; CABG = coronary artery bypass grafting; NR = not reported; RCT=randomized controlled trial; TIA = transient ischemic attack;

Appendix L

Strength of Evidence

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
Off-pump CABG vs. On-pump CABG	Clinical Outcomes (Dementia, CI)	RCT: 5 (5126) OBS: 1 (326)	RCT: Medium OBS: High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 4 (374)	Medium	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; No evidence for this outcome
	NP tests, Attention	RCT: 3 (250) OBS: 1 (326)	RCT: MediumOBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	RCT: 4 (374) OBS: 1 (326)	RCT: Medium OBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
	NP tests, Language	RCT: 3 (250) OBS: 1 (326)	RCT: MediumOBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
	NP tests, Executive	RCT: 5 (1420) OBS: 1 (326)	RCT: Medium OBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	RCT: 2 (190) OBS: 1 (326)	RCT: MediumOBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
	NP tests, Psychomotor speed	RCT: 2 (180) OBS: 1 (326)	RCT: Medium OBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	Neuropsychological tests, global cognitive screen	RCT: 1 (1273) OBS: 1 (326)	RCT: Medium OBS: High	Consistent	Imprecise	Direct	RCT: Low; No statistically significant differences OBS: Insufficient; Evidence has unacceptable deficiencies
On-pump CABG vs. Non-surgical control	Clinical Outcomes (Dementia, CI)	OBS: 1 (251)	High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	OBS: 1 (251)	High	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Attention	OBS: 1 (251)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	OBS: 1 (251)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Language	OBS: 1 (251)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Executive	OBS: 1 (251)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	OBS: 1 (251)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Psychomotor speed	OBS: 1 (251)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	OBS: 1 (251)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
Off-pump CABG vs. Non-surgical control	Clinical Outcomes (Dementia, CI)	OBS: 1 (174)	High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	OBS: 1 (174)	High	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Attention	OBS: 1 (174)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	OBS: 1 (174)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Language	OBS: 1 (174)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
							Insufficient; Evidence has

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	NP tests, Executive	OBS: 1 (174)	High	Unknown	Precise	Direct	unacceptable deficiencies
	NP tests, VSF	OBS: 1 (174)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Psychomotor speed	OBS: 1 (174)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	OBS: 1 (174)	High	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
On-pump CABG vs. CABG with Minimal Extracorporeal Bypass (MECC)[10]	Clinical Outcomes (Dementia, CI)	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low; Reduced risk (21 vs. 61%; RR=0.34 [CI, 0.16 to 0.73])
	NP tests, Attention	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low; MECC group scored statistically significantly better on WAIS digit symbol ES=1.08 [CI, 0.53 to 1.62]
	NP tests, Memory	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low; MECC group scored statistically significantly better on Fuld object memory evaluation.
	NP tests, Language	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Executive	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low, minimal extracorporeal bypass group scored statistically significantly better on Stroop Color/Word ES=0.89 [CI,0.36 to 1.42] WAIS digit span backward ES=0.94 [CI, 0.41 to 1.48]; WAIS digit symbol ES=1.08 [CI, 0.53 to 1.62]
	NP tests, VSF	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low, minimal extracorporeal bypass group scored statistically significantly better on

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
							Judgment of Line Orientation ES=0.98 [CI, 0.44 to 1.52]
	NP tests, Psychomotor speed	RCT: 1 (64)	Medium	Unknown	Precise	Direct	Low, minimal extracorporeal bypass group scored statistically significantly better on WAIS digit span backward ES=0.94 [CI, 0.41 to 1.48]; WAIS digit symbol ES=1.08 [CI, 0.53 to 1.62]
	Neuropsychological tests, global cognitive screen	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
Hypothermic vs. Normothermic[4, 6, 7]	Clinical Outcomes (Dementia, CI)	RCT: 3 (610)	Medium	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 3 (610)	Medium	Consistent	Imprecise	Direct	Low; No statistically significant differences
	NP tests, Attention	RCT: 3 (610)	Medium	Consistent	Imprecise	Direct	Low; No statistically significant differences
	NP tests, Memory	RCT: 2 (387)	Medium	Consistent	Imprecise	Direct	Low; No statistically significant differences
	NP tests, Language	RCT: 2 (387)	Medium	Consistent	Precise	Direct	Moderate; No statistically significant differences
	NP tests, Executive	RCT: 3 (610)	Medium	Consistent	Precise	Direct	Moderate; No statistically significant differences
	NP tests, VSF	RCT: 1 (120)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Psychomotor speed	RCT: 3 (610)	Medium	Consistent	Precise	Direct	Moderate; No statistically significant differences
	Neuropsychological tests, global cognitive screen		-	-	-	-	Insufficient; No evidence for this outcome
Anesthetic Regimen, High- vs. Low-dose Fentanyl[12,]	Clinical Outcomes (Dementia, CI)	RCT: 1 (350)	Medium	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (350)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	NP tests, Attention	RCT: 1 (350))	Medium	Unknown	Precise	Direct	Low; Evidence has unacceptable deficiencies
	NP tests, Memory	RCT: 1 (350)	Medium	Unknown	-	-	Insufficient; No evidence for this outcome
	NP tests, Language	RCT: 1 (350)	Medium	Unknown	Precise	Direct	Low; Evidence has unacceptable deficiencies
	NP tests, Executive	RCT: 1 (350)	Medium	Unknown	Precise	Direct	Low; Evidence has unacceptable deficiencies
	NP tests, VSF	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	RCT: 1 (350)	Medium	Unknown	Precise	Direct	Low; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	RCT: 1 (350)	Medium	-	-	-	Insufficient; No evidence for this outcome
Anesthetic Regimen, Propofol vs. Fentanyl [27]	Clinical Outcomes (Dementia, CI)	RCT: 1 (180)	Medium	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (180)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Attention	RCT: 1 (180))	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Memory	RCT: 1 (180)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Language	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Executive	RCT: 1 (180))	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, VSF	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	RCT: 1 (180)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	Neuropsychological tests, global cognitive screen	RCT: 1 (180)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
Miscellaneous Procedure Methods, Atmospheric Oxygen vs. Hyperbaric Oxygen[13]	Clinical Outcomes (Dementia, CI)	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (64)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Attention	RCT: 1 (64)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	RCT: 1 (64)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Language	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Executive	RCT: 1 (64)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	RCT: 1 (64)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	RCT: 1 (64)	Medium	-	-	-	Insufficient; No evidence for this outcome
Miscellaneous Procedure Methods, Cell Saver vs. Cardiotomy Suction[9]	Clinical Outcomes (Dementia, CI)	RCT: 1 (226)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (226)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Attention	RCT: 1 (226)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Memory	RCT: 1 (226)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Language	RCT: 1 (226)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Executive	RCT: 1 (226)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	RCT: 1 (226)	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	RCT: 1 (226)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	Neuropsychological tests, global cognitive screen	RCT: 1 (226)	Medium	-	-	-	Insufficient; No evidence for this outcome
Miscellaneous Procedure Methods, High Arterial Blood Pressure vs. Low Arterial Blood Pressure[15]	Clinical Outcomes (Dementia, CI)	RCT: 1 (248)	Medium	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (248)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Attention	RCT: 1 (248)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Memory	RCT: 1 (248)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Language	RCT: 1 (248)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	NP tests, Executive	RCT: 1 (248)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	RCT: 1 (248)	Medium	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	RCT: 1 (248)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	RCT: 1 (248)	Medium	-	-	-	Insufficient; No evidence for this outcome
Miscellaneous Procedure Methods, Candesartan (preoperative) vs. Placebo (preoperative)[11]	Clinical Outcomes (Dementia, CI)	RCT: 1 (106)	Unclear	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (106)	Unclear	**-**	**-**	**-**	Insufficient; No evidence for this outcome
	NP tests, Attention	RCT: 1 (106)	Unclear	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	RCT: 1 (106)	Unclear	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Language	RCT: 1 (106)	Unclear	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Executive	RCT: 1 (106)	Unclear	Unknown	Precise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	RCT: 1 (106)	Unclear	**-**	**-**	**-**	Insufficient; No evidence for this

Appendix L. Table 1. Strength of Evidence - CABG

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
							outcome
	NP tests, Psychomotor speed	RCT: 1 (106)	Unclear	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	RCT: 1 (106)	Unclear	-	-	-	Insufficient; No evidence for this outcome
CABG vs. Aortic or Mitral Valve Surgery Alone or in Combination with CABG[21]	Clinical Outcomes (Dementia, CI)	OBS: 1 (109)	High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	OBS: 1 (109)	High	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Attention	OBS: 1 (109)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Memory	OBS: 1 (109)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Language	OBS: 1 (109)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, Executive	OBS: 1 (109)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	NP tests, VSF	OBS: 1 (109)	High	-	-	-	Insufficient; No evidence for this outcome
	NP tests, Psychomotor speed	OBS: 1 (109)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	OBS: 1 (109)	High	-	-	-	Insufficient; No evidence for this outcome

Appendix L. Table 2. Strength of Evidence - AVR

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
AVR under hypothermia vs. AVR under normothermia[18]	Clinical Outcomes (Dementia, CI)	RCT: 1 (60)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (60)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Attention	RCT: 1 (60)	Medium	Unknown	Unclear**	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, Memory	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Language	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Executive	RCT: 1 (60)	Medium	Unknown	Unclear**	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, VSF	-	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Psychomotor speed		Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, global cognitive screen	RCT: 1 (60)	Medium	Unknown	Unclear**	Direct	Insufficient; Evidence has unacceptable deficiencies
AVR vs. Transapical transcatheter aortic valve implantation	Clinical Outcomes (Dementia, CI)	OBS: 1 (64)	High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	OBS: 1 (64)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, Attention			-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Memory			-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Language			-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological						Insufficient;

Appendix L. Table 2. Strength of Evidence - AVR

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	tests, Executive			-	-	-	No evidence for this outcome
	Neuropsychological tests, VSF			-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Psychomotor speed			-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, global cognitive screen			-	-	-	Insufficient; No evidence for this outcome

CAS = Carotid artery stenting; CEA = Carotid endarterectomy; CI = cognitive impairment; OBS = prospective observational cohort study; RCT = randomized controlled trial; VSF = visual-spatial functioning

*Strength of the evidence was evaluated based on the following domains: (1) study limitations (risk of bias or internal validity); (2) directness; (3) consistency; (4) precision; and, when appropriate, (5) reporting bias. Study limitations will be rated as low, medium or high based on the study design and risk of bias of individual studies.

**Though the Fakin study reports that they collected Trails A, Trails B and MMSE at baseline and follow-up, the study reported insufficient detail on these results quantify within or between-group changes in these outcomes. Precision could not be determined.

Appendix L. Table 3. Strength of Evidence for CAS / CEA studies

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
CEA vs. CAS[16]	Clinical Outcomes (Dementia, CI)	RCT: 1 (177)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"	RCT: 1 (177)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Attention	RCT: 1 (177)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, Memory	RCT: 1 (177)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	Neuropsychological tests, Language	RCT: 1 (177)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	Neuropsychological tests, Executive	RCT: 1 (177)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	Neuropsychological tests, VSF	RCT: 1 (177)	Medium	Unknown	Precise	Direct	Low; No statistically significant differences
	Neuropsychological tests, Psychomotor speed	RCT: 1 (177)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, global cognitive screen	RCT: 1 (177)	Medium	-	-	-	Insufficient; No evidence for this outcome
CEA vs. Angioplasty[17]	Clinical Outcomes (Dementia, CI)	RCT: 1 (46)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"		Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, Attention	RCT: 1 (46)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, Memory	RCT: 1 (46)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies

Appendix L. Table 3. Strength of Evidence for CAS / CEA studies

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	Neuropsychological tests, Language	RCT: 1 (46)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Executive	RCT: 1 (46)	Medium	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, VSF	RCT: 1 (46)	Medium	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Psychomotor speed	RCT: 1 (46)	Medium	Consistent	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies
	Neuropsychological tests, global cognitive screen	RCT: 1 (46)	Medium	-	-	-	Insufficient; No evidence for this outcome
CEA vs. laparoscopic cholecystectomy control[22]	Clinical Outcomes (Dementia, CI)	OBS: 1 (227)	High	-	-	-	Insufficient; No evidence for this outcome
	Composite NP test "impairment"		High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Attention	-	High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Memory	-	High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Language	-	High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Executive	-	High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, VSF	-	High	-	-	-	Insufficient; No evidence for this outcome
	Neuropsychological tests, Psychomotor	-	High	-	-	-	Insufficient; No evidence for this outcome

Appendix L. Table 3. Strength of Evidence for CAS / CEA studies

Comparison	Outcome	Study design: No. studies (N)	Study Limitations	Consistency	Precision	Directness	SOE Grade*: Finding
	speed						
	Neuropsychological tests, global cognitive screen	OBS: 1 (227)	High	Unknown	Imprecise	Direct	Insufficient; Evidence has unacceptable deficiencies

*Strength of the evidence was evaluated based on the following domains: (1) study limitations (risk of bias or internal validity); (2) directness; (3) consistency; (4) precision; and, when appropriate, (5) reporting bias. Study limitations will be rated as low, medium or high based on the study design and risk of bias of individual studies.

CAS = Carotid artery stenting; CEA = Carotid endarterectomy; CI = cognitive impairment; OBS = prospective observational cohort study; RCT = randomized controlled trial; VSF = visual-spatial functioning

Appendix M

Mean Change from Baseline Tables

Appendix M. Mean change from baseline tables

Table 1. Mean change from baseline for Trail Making A (time in seconds), CABG studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Vedin 2006[3] /	6	CABG, off-pump	34 (11.5); n=33	32.0 (8.2); n=30	-2.0 [-6.9 to 2.9]	0.20 [-0.30 to 0.69]	0.09 [-0.41 to 0.59]
Randomized trial	6	CABG, on-pump	37 (16.7); n=37	34.0 (7.1); n=32	-3.0 [-8.9 to 2.9]	0.23 [-0.25 to 0.70]	
Lee 2003[5] /	12	CABG, off-pump	47.4 (22.2); n=30	45.7 (15.2); n=27	-1.7 [-11.5 to 8.1]	0.09 [-0.43 to 0.61]	-0.05 [-0.59 to 0.49]
Randomized trial	12	CABG, on-pump	43.7 (32.6); n=30	43.4 (34.4); n=26	-0.3 [-17.9 to 17.3]	0.01 [-0.52 to 0.53]	
Selnes 2009[20] /	12	CABG, off-pump	48.0 (23.0); n=69	43.4 (17.5); n=55	-4.6 [-11.7 to 2.5]	0.22 [-0.14, 0.58]	Off vs. On 0.08 [-0.24 to 0.40]
Prospective observational	12	CABG, on-pump	47.1 (24.2); n=151	40.8 (16.8); n=123	-6.3 [-11.2 to -1.4]	0.30 [0.06 to 0.54]	Off vs. NSC -0.15 [-0.48 to 0.19]
	12	Non-surgical control	43.1 (14.4); n=99	41.0 (15.6); n=91	-2.1 [-6.4 to 2.2]	0.14 [-0.15 to 0.42]	On vs. NSC -0.23 [-0.50 to 0.05]
	72	CABG, off-pump	48.0 (23.0); n=69	42.6 (15.9); n=43	-5.4 [-12.6 to 1.8]	0.26 [-0.12 to 0.64]	Off vs. On -0.24 [-0.60 to 0.13]
	72	CABG, on-pump	47.1 (24.2); n=151	47.7 (29.5); n=95	0.6 [-6.5 to 7.7]	-0.02 [-0.28 to 0.23]	Off vs. NSC -0.37 [-0.76 to 0.02]
	72	Non-surgical control	43.1 (14.4); n=99	46.4 (31.6); n=67	3.3 [-4.8 to 11.4]	-0.14 [-0.45 to 0.17]	On vs. NSC -0.10 [-0.41 to 0.21]
Nathan, 2001[7] /	60	CABG, hypothermic	38.7 (11.5); n=65	NR	6.5 (19.0); n=65	NA	0.27 [-0.08 to 0.61]
Randomized trial	60	CABG, normothermic	39.9 (11.6); n=66	NR	2.9 (1.8); n=66	NA	
Boodhwani 2007[6] /	3	CABG, hypothermic	41.9 (14.8); n=133	NR	-4.0 (12.3); n=119	NA	-0.21 [-0.47 to 0.04]
Randomized trial	3	CABG, normothermic	40.2 (12.3); n=134	NR	-1.4 (11.9); n=117	NA	
Alex 2005[13] /	4	CABG, atmos. air	41.7 (14.9); n=31	40.6 (15.7); n=31	-1.1 [-8.7 to 6.5]	0.07 [-0.43 to 0.57]	0.03 [-0.46 to 0.52]
Randomized trial	4	CABG, oxygen	43.0 (16.3); n=33	41.4 (15.5); n=33	-1.6 [-9.3 to 6.1]	0.10 [-0.38 to 0.58]	
Flesch 2009[11] /	3	CABG, cardesartan	43.2 (10.9); n=53	44.1 (14.5); n=43	0.9 [-4.3 to 6.1]	-0.07 [-0.47 to 0.33]	-0.33 [-0.75 to 0.10]
Randomized trial	3	CABG, placebo	42.6 (10.7); n=53	47.2 (10.1); n=44	4.6 [0.5 to 8.8]	-0.44 [-0.84 to -0.03]	
Gold 1995[15] /	6	CABG, low MAP	43.7 (22.3); n=124	NR	-2.7 (15.4); n=113	NA	0.07 [-0.19 to 0.33]

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Randomized trial	6	CABG, high MAP	45.2 (24.7); n=124	NR	-4.0 (20.3); n=112	NA	
Kadoi 2003[14] / Randomized trial	6	CABG, propofol	42.5 (6.6); n=77	44.1 (5.7); n=77	1.6 [-0.4 to 3.6]	-0.26 [-0.58 to 0.06]	-0.10 [-0.41 to 0.22]
	6	CABG, fentanyl	43.2 (5.6); n=75	45.4 (6.9); n=75	2.2 [0.2 to 4.2]	-0.35 [-0.67 to -0.03]	
Silbert 2006[12] / Randomized trial	12	CABG, low-dose fentanyl	55.0 (25.7); n=168	48.0 (18.1); n=159	-7 [-11.8 to -2.2]	0.31 [0.09 to 0.53]	-0.14 [-0.37 to 0.08]
	12	CABG, high-dose fentanyl	54.6 (23.6); n=158	50.8 (22.6); n=140	-3.8 [-9.1 to 1.5]	0.16 [-0.06 to 0.39]	

CI = confidence intervals; ES = effect size; PO = prospective observational study; RCT = randomized controlled trial; MAP = mean arterial pressure (during bypass); NSC = non-surgical control

Table 2. Mean change from baseline for Trail Making A (time in seconds), Carotid artery stenting (CAS) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	Carotid PTA	47.0 (17.0); n=20	46.3 (19.5); n=18	-0.7 [-12.4 to 11.0]	0.04 [-0.60 to 0.67]	-0.28 [-0.91 to 0.35]
	6	CEA	68.8 (57.4); n=26	88.3 (119.4); n=22	19.5 [-35.1 to 74.1]	-0.21 [-0.78 to 0.36]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation;

Table 3. Mean change from baseline for Trail Making A (time in seconds), Carotid endarterectomy (CEA) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	CEA	68.8 (57.4); n=26	88.3 (119.4); n=22	19.5 [-35.1 to 74.1]	-0.21 [-0.78 to 0.36]	0.28 [-0.35 to 0.91]
	6	Carotid PTA	47.0 (17.0); n=20	46.3 (19.5); n=18	-0.7 [-12.4 to 11.0]	0.04 [-0.60 to 0.67]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation

Appendix M. Mean change from baseline tables

Table 4. Mean change from baseline for Verbal Fluency, CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Vedin, 2006[3] /		CABG,					
COWAT	6	off-pump	30 (10.1); n=33	30 (5.8); n=30	0.0 [-4.0 to 4.0]	0.00 [-0.49 to 0.49]	-0.56 [-1.06 to -0.05]
Randomized trial		CABG,					
	6	on-pump	25 (7.6); n=37	29 (5.7); n=32	4 [0.9 to 7.2]	-0.58 [-1.07 to -0.10]	
Lund, 2005[4] /		CABG,					
COWAT	12	off-pump	34.0 (11.3); n=60	36.0 (13.3); n=54	2.0 [-2.6 to 6.6]	-0.16 [-0.53 to 0.21]	-0.02 [-0.40 to 0.36]
Randomized trial		CABG,					
	12	off-pump	36.4 (11.2); n=60	38.6 (12.0); n=52	2.2 [-2.1 to 6.5]	-0.19 [-0.56 to 0.18]	
Djaiani, 2012[9] /		CABG with					
	12	cell-saver	36.4 (12.6); n=85	38.1 (12.2); n=85	1.7 [-2.0 to 5.4]	-0.14 [-0.44 to 0.16]	-0.04 [-0.34 to 0.26]
Randomized trial		CABG					
	12	with suction	34.8 (10.6); n=83	37.0 (11.2); n=83	2.2 [-1.1 to 5.5]	-0.20 [-0.51 to 0.10]	
Boodhwani, 2007[6] /	3	CABG, hypothermic	31.7 (12.1); n=133	NR	2.6 (7.2); n=119	NA	0.21 [-0.05 to 0.46]
Randomized trial	3	CABG, normothermic	32.2 (12.4); n=134	NR	1.0 (8.1); n=117	NA	
Flesch, 2009[11] /		CABG,					
	3	cardesartan	61.7 (9.6); n=53	61.9 (10.8); n=43	-0.20 [-4.34 to 3.94]	-0.02 [-0.42 to 0.38]	0.04 [-0.38 to 0.46]
Randomized trial		CABG,					
	3	placebo	57.8 (12.8); n=53	58.5 (12.9); n=44	-0.70 [-5.84 to 4.44]	-0.05 [-0.45 to 0.35]	
Gold, 1995[15] /		CABG,					
COWAT	6	low MAP	37.5 (13.1) ; n=124	NR	0.0 (8.3) n=113	NA	-0.08 [-0.34 to 0.18]
Randomized trial		CABG,					
	6	high MAP	37.6 (13.4); n=124	NR	0.6 (6.1) n=112	NA	
Silbert, 2006[12] /		CABG,					
COWAT	12	low-dose	33.1 (12.3); n=168	35.3 (12.0); n=159	2.2 [-0.4 to 4.8]	-0.18 [-0.40 to 0.04]	0.02 [-0.21 to 0.24]
Randomized trial		fentanyl					
		CABG,					
	12	high-dose	31.4 (11.3); n=158	33.4 (12.9); n=141	2.0 [-0.8 to 4.8]	-0.17 [-0.39 to 0.06]	
		fentanyl					

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

Appendix M. Mean change from baseline tables

Table 5. Mean change from baseline for Rey Auditory Verbal Learning Test (number of words), CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lund 2005[4] /		CABG,					
	12	off-pump	33.6 (8.9); n=60	37.4 (10.7); n=54	3.8 [0.16 to 7.4]	-0.39 [-0.76 to -0.01]	-0.26 [-0.63 to 0.11]
Randomized trial		CABG,					
	12	off-pump	35.7 (7.9); n=60	41.8 (7.9); n=52	6.1 [9.0 to 3.2]	-0.77 [-1.15 to -0.38]	
Lee 2003[5] /		CABG,					
	12	off-pump	36.1 (13.1); n=30	42.9 (12.0); n=27	6.8 [0.28 to 13.3]	-0.53 [-1.06 to -0.00]	0.17 [-0.35 to 0.69]
Randomized trial		CABG,					
	12	on-pump	39.2 (16.1); n=30	43.7 (14.8); n=26	4.5 [-3.6 to 12.6]	-0.29 [-0.81 to 0.24]	
Selnes 2009[20] /		CABG,					Off vs. On
	12	off-pump	38.5 (9.2); n=72	42.3 (10.3); n=55	3.8 [0.4 to 7.3]	-0.39 [-0.74 to -0.04]	-0.17 [-0.49 to 0.14]
Prospective		CABG,					Off vs. NSC
observational	12	on-pump	39.1 (8.8); n=152	44.6 (10.6); n=124	5.5 [3.2 to 7.8]	-0.57 [-0.81 to -0.33]	-0.05 [-0.39 to 0.28]
		Non-surgical					On vs. NSC
	12	control	41.2 (8.8); n=99	45.5 (10.4); n=91	4.3 [1.6 to 7.1]	-0.45 [-0.73 to -0.16]	0.12 [-0.15 to 0.40]
		CABG,					Off vs. On
	72	off-pump	38.5 (9.2); n=72	40.0 (11.2); n=43	1.5 [-2.5 to 5.5]	-0.15 [-0.53 to 0.23]	0.12 [-0.24 to 0.48]
		CABG,					Off vs. NSC
	72	on-pump	39.1 (8.8); n=152	39.4 (10.4); n=96	0.3 [-2.2 to 2.8]	-0.03 [-0.29 to 0.22]	-0.02 [-0.40 to 0.36]
		Non-surgical					On vs. NSC
	72	control	41.2 (8.8); n=99	42.9 (11.6); n=67	1.7 [-1.6 to 5.0]	-0.17 [-0.48 to 0.14]	-0.15 [-0.46 to 0.17]
Djaiani 2012[9] /		CABG with					
	12	cell-saver	7.0 (2.9); n=84	7.2 (3.4); n=84	0.2 [-0.8 to 1.2]	-0.06 [-0.37 to 0.24]	0.16 [-0.15 to 0.46]
Randomized trial		CABG					
	12	with suction	7.7 (2.9); n=84	7.4 (3.1); n=84	-0.3 [-1.2 to 0.6]	0.10 [-0.20 to 0.40]	
Boodhwani 2007[6]/		CABG,					
	3	hypothermic	37.8 (9.2); n=133	NR	0.3 (7.1); n=119	NA	0.18 [-0.08 to 0.43]
Randomized trial		CABG,					
	3	normothermic	38.4 (9.6); n=134	NR	-1.0 (7.6) n=117	NA	
Alex 2005[13] /		CABG,					
	4	atmos. air	41.2 (9.6); n=31	40.6 (10.4); n=31	-0.6 [-5.6 to 4.4]	0.06 [-0.44 to 0.56]	-0.21 [-0.70 to 0.28]
Randomized trial		CABG,					
	4	oxygen	37.8 (11.5); n=33	39.4 (11): n=33	1.6 [-7.0 to 3.8]	-0.14 [-0.62 to 0.34]	
Kadoi 2003[27] /		CABG,	Immediate recall	Immediate recall			
	6	propofol	40.6 (6.6); n=77	43.1 (7.7); n=77	2.5 [0.2 to 4.8]	-0.35 [-0.67 to -0.03]	0.01 [-0.31 to 0.33]
Randomized trial		CABG,	Immediate recall	Immediate recall			
	6	fentanyl	42.7 (5.6); n=75	45.1 (11.7); n=75	2.4 [-0.5 to 5.3]	-0.26 [-0.58 to 0.06]	
		CABG,	delayed recall	delayed recall		-0.59 [-0.91 to -0.27]	

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
	6	propofol	22.4 (3.9); n=77	25.2 (5.4); n=77	2.8 [1.3 to 4.3]		0.06 [-0.26 to 0.37]
	6	CABG, fentanyl	delayed recall 23.1 (3.5); n=75	delayed recall 25.6 (7.7); n=75	2.5 [0.6 to 4.4]	-0.42 [-0.74 to -0.09]	

CI = confidence intervals; ES = effect size; PO = prospective observational study; RCT = randomized controlled trial; MAP = mean arterial pressure (during bypass); NSC = non-surgical control

Table 6. Mean change from baseline for Rey Auditory Verbal Learning Test (number of words), Carotid artery stenting (CAS) studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	Carotid PTA	53.2 (12.3); n=20	53.9 (16.8); n=18	0.7 [-8.8 to 10.2]	-0.05 [-0.68 to 0.59]	-0.08 [-0.71 to 0.54]
	6	CEA	53.9 (12.8); n=26	55.8 (14.9); n=22	1.9 [-6.0 to 9.8]	-0.14 [-0.70 to 0.43]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation

Table 7. Mean change from baseline for Rey Auditory Verbal Learning Test (number of words), Carotid endarterectomy (CEA) studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	CEA	53.9 (12.8); n=26	55.8 (14.9); n=22	1.9 [-6.0 to 9.8]	-0.14 [-0.70 to 0.43]	0.08 [-0.54 to 0.71]
	6	Carotid PTA	53.2 (12.3); n=20	53.9 (16.8); n=18	0.7 [-8.8 to 10.2]	-0.05 [-0.68 to 0.59]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation deviation

Appendix M. Mean change from baseline tables

Table 8. Mean change from baseline for Trail Making B (time in seconds), CABG studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lamy, 2013[1] /	12	CABG, off-pump	158.0 (88.1); n=721	NR	-6.8 (64.0); n=353	NA	-0.05 [-0.20 to 0.10]
Randomized trial	12	CABG, on-pump	163.7 (89.5); n=711	NR	-3.2 (70.2); n=340	NA	
Jensen 2008[2] /	12	CABG, off-pump	61.7 (24.9); n=61	66.7 (27.0); n=47	-5.00 [-14.93 to 4.93]	-0.19 [-0.57 to 0.19]	-0.17 [-0.58 to 0.25]
Randomized trial	12	CABG, on-pump	63.6 (23.4); n=59	64.4 (25.1); n=43	-0.80 [-10.39, 8.79]	-0.03 [-0.43 to 0.36]	
Vedin, 2006[3] /	6	CABG, off-pump	82 (28.7); n=33	84 (9.6); n=30	2.0 [-8.4 to 12.4]	-0.09 [-0.59 to 0.40]	0.70 [0.19 to 1.22]
Randomized trial	6	CABG, on-pump	104 (54.7); n=37	83 (25.5); n=32	-21 [-40.7 to -1.3]	0.48 [-0.00 to 0.96]	
Lee, 2003[5] /	12	CABG, off-pump	126.0 (86.7); n=30	117.3 (63.4); n=27	-8.7 [-47.9 to 30.5]	0.11 [-0.41 to 0.63]	0.02 [-0.52 to 0.56]
Randomized trial	12	CABG, on-pump	114.9 (87.6); n=30	104.4 (92.1); n=26	-10.5 [-57.8 to 36.8]	0.12 [-0.41 to 0.64]	
Selnes, 2009[20] /	12	CABG, off-pump	96.9 (34.7); n=68	97.2 (48.4); n=55	0.3 [-14.9 to 15.5]	-0.01 [-0.36 to 0.35]	Off vs. On 0.20 [-0.12 to 0.52]
Prospective observational	12	CABG, on-pump	105.2 (59.0); n=147	95.4 (48.2); n=122	-9.8 [-22.6 to 3.0]	0.18 [-0.06 to 0.42]	Off vs. NSC 0.09 [-0.24 to 0.43]
	12	Non-surgical control	95.4 (40.0); n=99	92.0 (41.5); n=91	-3.4 [-15.0 to 8.2]	0.08 [-0.20 to 0.37]	On vs. NSC -0.13 [-0.40 to 0.14]
	72	CABG, off-pump	96.9 (34.7); n=68	101.4 (47.1); n=43	4.5 [-11.8 to 20.8]	-0.11 [-0.49, 0.27]	Off vs. On 0.09 [-0.27 to 0.45]
	72	CABG, on-pump	105.2 (59.0); n=147	105.0 (50.1); n=91	-0.2 [-14.2 to 13.8]	0.00 [-0.26 to 0.27]	Off vs. NSC -0.01 [-0.40 to 0.37]
	72	Non-surgical control	95.4 (40.0); n=99	100.4 (50.6); n=66	5.0 [-9.5 to 19.5]	-0.11 [-0.42 to 0.20]	On vs. NSC -0.10 [-0.42 to 0.21]
Nathan, 2001[7] /	60	CABG, hypothermic	104.3 (46.7); n=65	NR	24.2 (47.8); n=65	NA	0.22 [-0.12 to 0.56]
Randomized trial	60	CABG, normothermic	103.7 (9.2); n=66	NR	14.1 (43.6); n=66	NA	
Boodhwani, 2007[6] /	3	CABG, hypothermic	105.6 (45.0); n=133	NR	-11.7 (29.0); n=119	NA	-0.12 [-0.38 to 0.14]
Randomized trial	3	CABG, normothermic	103.3 (43.3); n=134	NR	-7.8 (35.5); n=117	NA	
Alex, 2005[13] /	4	CABG, atmos. air	101 (43.5); n=31	107 (54.7); n=31	6.0 [-18.6 to 30.6]	-0.12 [-0.62 to 0.38]	0.50 [0.00 to 1.00]
Randomized trial		CABG,					

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
	4	oxygen	127.1 (52.6); n=33	108.7 (45.5); n=33	-18.4 [-42.1 to 5.3]	0.37 [-0.12 to 0.86]	
Flesch, 2009[11] / Randomized trial	3	CABG, cardesartan	40.5 (10.1); n=53	44.8 (11.3); n=43	4.3 [-0.04 to 8.6]	-0.40 [-0.81 to 0.01]	-0.05 [-0.47 to 0.37]
	3	CABG, placebo	40.7 (10.9); n=53	45.5 (12.8); n=44	4.8 [0.01 to 9.6]	-0.40 [-0.81 to 0.00]	
Gold, 1995[15] / Randomized trial	6	CABG, low MAP	104.6 (60.8); n=124	NR	-3.6 (46.9); n=113	NA	0.24 [-0.03 to 0.50]
	6	CABG, high MAP	102.6 (49.3); n=124	NR	-13.9 (39.3); n=112	NA	
Kadoi, 2003[27] / Randomized trial	6	CABG, propofol	154.2 (51.1); n=77	164.0 (63.4); n=77	9.8 [-8.4 to 28.0]	-0.17 [-0.49 to 0.15]	-0.18 [-0.49 to 0.14]
	6	CABG, fentanyl	156.3 (50.3); n=75	176.0 (57.0); n=75	19.7 [2.5 to 36.9]	-0.36 [-0.69 to -0.04]	
Silbert, 2006[12] / Randomized trial	12	CABG, low-dose fentanyl	125.7 (62.5); n=168	110.5 (58.1); n=158	-15.2 [-28.3 to -2.1]	0.25 [0.03 to 0.47]	-0.08 [-0.31 to 0.15]
	12	CABG, high-dose fentanyl	127.5 (62.4); n=158	117.1 (58.9); n=141	-10.4 [-24.2 to 3.4]	0.17 [-0.06 to 0.40]	

CI = confidence intervals; ES = effect size; MAP = mean arterial pressure (during bypass); NSC = non-surgical control; SD = standard deviation

Table 9. Mean change from baseline for Trail Making B (time in seconds), Carotid artery stenting (CAS) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	Carotid PTA	129.5 (76.8); n=20	152.9 (113.7); n=18	23.4 [-39.0 to 85.8]	-0.24 [-0.88 to 0.40]	0.26 [-0.37 to 0.88]
	6	CEA	144.0 (49.2); n=26	147.0 (70.6); n=22	3.0 [-32.0 to 38.0]	-0.05 [-0.62 to 0.52]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation

Appendix M. Mean change from baseline tables

Table 10. Mean change from baseline for Trail Making B (time in seconds), Carotid endarterectomy (CEA) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	CEA	144.0 (49.2); n=26	147.0 (70.6); n=22	3.0 [-32.0 to 38.0]	-0.05 [-0.62 to 0.52]	-0.26 [-0.88 to 0.37]
	6	Carotid PTA	129.5 (76.8); n=20	152.9 (113.7); n=18	23.4 [-39.0 to 85.8]	-0.24 [-0.88, 0.40]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation;

Table 11. Mean change from baseline for Grooved Pegboard Test (seconds), CABG studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lund, 2005[4] / Randomized trial	12	CABG, off-pump	84.5 (19.3); n=60	78.8 (16.8); n=54	-5.7 [-12.3 to 0.9]	0.31 [-0.06 to 0.68]	-0.19 [-0.57 to 0.19]
	12	CABG, off-pump	81.3 (16.9); n=60	78.8 (16.1); n=52	-2.5 [-8.6 to 3.6]	0.15 [-0.22, 0.52]	
Lee 2003[5] / Randomized trial	12	CABG, off-pump	Dominant 97.8 (30.7); n=30	Dominant 91.5 (26.0); n=27	-6.3 [-21.0 to 8.4]	0.22 [-0.30 to 0.74]	-0.03 [-0.57 to 0.51]
	12	CABG, on-pump	Dominant 96.8 (46.9); n=30	Dominant 91.5 (26.0); n=26	-5.3 [-24.8 to 14.2]	0.14 [-0.39 to 0.66]	
	12	CABG, off-pump	Non-dominant 100.9 (124.5); n=30	Non-dominant 97.6 (32.2); n=27	-3.3 [-49.5 to 42.3]	0.03 [-0.49 to 0.55]	-0.19 [-0.57 to 0.19]
	12	CABG, on-pump	Non-dominant 97.2 (37.2); n=30	Non-dominant 89.6 (29.6); n=26	-7.6 [-25.1 to 9.9]	0.22 [-0.31 to 0.75]	
Selnes 2009[20] / Prospective observational	12	CABG, off-pump	Dominant 99.6 (30.9); n=67	Dominant 94.2 (32.1); n=54	-5.4 [-16.7 to 5.9]	0.17 [-0.19 to 0.53]	Off vs. On 0.16 [-0.16 to 0.48]
	12	CABG, on-pump	Dominant 107.5 (53.7); n=152	Dominant 95.6 (29.9); n=122	-11.9 [-1.9 to -22.0]	0.27 [0.03 to 0.50]	Off vs. NSC 0.06 [-0.28 to 0.40]
	12	Non-surgical control	Dominant 97.9 (29.7); n=99	Dominant 90.8 (24.6); n=91	-7.1 [-14.8 to 0.6]	0.26 [-0.03 to 0.54]	On vs. NSC -0.13 [-0.40 to 0.14]
	12	CABG, off-pump	Non-dominant 107.0 (34.4); n=68	Non-dominant 98.1 (30.3); n=54 54	-8.9 [-20.4 to 2.6]	0.27 [-0.09 to 0.63]	Off vs. On 0.17 [-0.16 to 0.49]
	12	CABG, on-pump	Non-dominant 119.1 (65.3); n=149	Non-dominant 103.4 (30.6); n=123	-15.7 [-27.5 to -3.9]	0.30 [0.06 to 0.54]	Off vs. NSC -0.11 [-0.45 to 0.23]
	12	Non-surgical control	Non-dominant 107.4 (38.4); n=98	Non-dominant 102.5 (35.6); n=89	-4.9 [-15.5 to 5.7]	0.13 [-0.16 to 0.42]	On vs. NSC -0.26 [-0.54 to 0.01]
		CABG,	Dominant	Dominant	-3.6 [-16.3 to 9.1]	0.11 [-0.27 to 0.49]	Off vs. On

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
	72	off-pump	99.6 (30.9); n=67	96.0 (34.4); n=43			-0.04 [-0.40 to 0.32]
		CABG,	Dominant	Dominant			Off vs. NSC
	72	on-pump	107.5 (53.7);n=152	105.5 (36.0); n=93	-2.0 [-13.2 to 9.2]	0.04 [-0.22 to 0.30]	-0.25 [-0.64 to 0.13]
		Non-surgical	Dominant	Dominant			On vs. NSC
	72	control	97.9 (29.7); n=99	103.3 (42.0); n=67	5.4 [-6.2 to 17.0]	-0.15 [-0.46 to 0.16]	-0.18 [-0.49 to 0.13]
		CABG,	Non-dominant	Non-dominant			Off vs. On
	72	off-pump	107.0 (34.4); n=68	99.0 (30.4); n=43	-8.0 [-20.2 to 4.2]	0.24 [-0.14 to 0.62]	-0.11 [-0.47 to 0.25]
		CABG,	Non-dominant	Non-dominant			Off vs. NSC
	72	on-pump	119.1 (65.3); n=149	116.3 (41.3); n=94	-2.8 [-16.2 to 10.6]	0.05 [-0.21 to 0.31]	-0.32 [-0.71 to 0.06]
		Non-surgical	Non-dominant	Non-dominant			On vs. NSC
	72	control	107.4 (38.4); n=98	111.6 (42.9); n=66	4.2 [-8.6 to 17.0]	-0.10 [-0.42 to 0.21]	-0.15 [-0.46 to 0.17]
Djaiani 2012[9] /		CABG with					
	12	cell-saver	90.0 (18.7); n=84	89.1 (18.8); n=84	-0.9 [-6.6 to 4.8]	0.05 [-0.25 to 0.35]	0.20 [-0.10 to 0.51]
Randomized trial		CABG					
	12	with suction	91.3 (21.9); n=83	86.1 (23.4); n=83	-5.2 [-12.1 to 1.7]	0.23 [-0.08 to 0.53]	
Boodhwani 2007[6] /		CABG,	Dominant	Dominant			
	3	hypothermic	90.1 (20.5); n=133	NR	-4.0 (13.4); n=119	NA	-0.14 [-0.40 to 0.11]
Randomized trial		CABG,	Dominant	Dominant			
	3	normothermic	91.1 (24.4); n=134	NR	-2.0 (14.8); n=117	NA	
		CABG,	Non-dominant	Non-dominant			
	3	hypothermic	99.2 (26.6); n=133	NR	-4.3 (18.2); n=119	NA	-0.05 [-0.30 to 0.21]
		CABG,	Non-dominant	Non-dominant			
	3	normothermic	100.1 (28.3); n=134	NR	-3.5 (13.7); n=117	NA	
Nathan 2001[7] /		CABG,					
	60	hypothermic	88.2 (17.0); n=65	NR	14.7 (30.7); n=65	NA	0.04 [-0.31 to 0.38]
Randomized trial		CABG,					
	60	normothermic	87.5 (20.7); n=66	NR	13.7 (21.6); n=66	NA	
Alex 2005 /		CABG,	Dominant	Dominant			
	4	atmos. air	19.1 (2.2); n=31	19.1 (2.6); n=31	0.0 [-1.2 to 1.2]	0.00 [-0.50 to 0.50]	0.24 [-0.26 to 0.73]
Randomized trial		CABG,	Dominant	Dominant			
	4	oxygen	19.7 (2.8); n=33	19.1 (2.5); n=33	-0.6 [-1.9 to 0.7]	0.22 [-0.26 to 0.71]	
		CABG,	Non-dominant	Non-dominant			
	4	atmos. air	21.0 (2.3); n=31	20.4 (2.6); n=31	-0.6 [-1.8 to 0.6]	0.24 [-0.26 to 0.74]	-0.17 [-0.67 to 0.32]
		CABG,	Non-dominant	Non-dominant			
	4	oxygen	21.0 (3.0); n=33	20.9 (3.7); n=33	-0.1 [-1.7 to 1.5]	0.03 [-0.45 to 0.51]	
Kadoi 2003[27] /		CABG,					
	6	propofol	21.9 (3.0); n=77	23.2 (4.0); n=77	1.3 [0.2 to 2.4]	-0.37 [-0.68 to -0.05]	0.03 [-0.29 to 0.34]
Randomized trial		CABG,					
	6	fentanyl	22.0 (3.5); n=75	23.2 (4.3); n=75	1.2 [-0.1 to 2.5]	-0.30 [-0.63 to 0.02]	
Silbert 2006[12] /		CABG,	Dominant	Dominant	-9.1 [-15.8 to -2.4]	0.30 [0.08 to 0.52]	0.05 [-0.18 to 0.27]

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Randomized trial	12	low-dose fentanyl	99.7 (30.6); n=165	90.6 (30.7); n=155			
	12	CABG, high-dose fentanyl	Dominant 102.1 (34.5); n=155	Dominant 91.6 (28.0); n=138	-10.5 [-17.7 to -3.3]	0.33 [0.10 to 0.56]	
	12	CABG, low-dose fentanyl	Non-dominant 110.2 (39.2); n=166	Non-dominant 100.1 (34.3); n=155	-10.1 [-18.1 to -2.1]	0.27 [0.05 to 0.49]	-0.01 [-0.24 to 0.22]
	12	CABG, high-dose fentanyl	Non-dominant 108.5 (37.8); n=152	Non-dominant 98.6 (22.3); n=136	-9.9 [-17.0 to -2.8]	0.31 [0.08 to 0.55]	

CI = confidence intervals; ES = effect size; NSC = non-surgical control; SD = standard deviation

Table 12. Mean change from baseline for Grooved Pegboard Test (seconds), Carotid artery stenting (CAS) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	Carotid PTA	Dominant 89.3 (21.8); n=20	Dominant 103.8 (34.3); n=18	14.5 [-4.0 to 33.0]	-0.50 [-1.15 to 0.15]	0.37 [-0.26 to 1.00]
	6	CEA	Dominant 106.6 (33.6); n=26	Dominant 108.8 (39.6); n=22	2.2 [-18.8 to 23.2]	-0.06 [-0.63 to 0.51]	
	6	Carotid PTA	Non-dominant 109.4 (32.2); n=20	Non-dominant 120.4 (47.8); n=18	11.0 [-15.2 to 37.2]	-0.27 [-0.91 to 0.37]	-0.05 [-0.67 to 0.58]
	6	CEA	Non-dominant 113.3 (26.3); n=26	Non-dominant 126.5 (65.7); n=22	13.2 [-16.1 to 42.5]	-0.27 [-0.84 to 0.30]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation

Table 13. Mean change from baseline for Grooved Pegboard Test (seconds), Carotid endarterectomy (CEA) studies. *Lower scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
Crawley 2000[17] / Randomized trial	6	CEA	Dominant 106.6 (33.6); n=26	Dominant 108.8 (39.6); n=22	2.2 [-18.8 to 23.2]	-0.06 [-0.63 to 0.51]	-0.37 [-1.00 to 0.26]
			Dominant	Dominant	14.5 [-4.0 to 33.0]	-0.50 [-1.15 to 0.15]	

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n*	ES [95%CI] within groups	ES [95%CI] between groups
	6	Carotid PTA	89.3 (21.8); n=20	103.8 (34.3); n=18			
	6	CEA	Non-dominant 113.3 (26.3); n=26	Non-dominant 126.5 (65.7); n=22	13.2 [-16.1 to 42.5]	-0.27 [-0.84 to 0.30]	0.05 [-0.58 to 0.67]
	6	Carotid PTA	Non-dominant 109.4 (32.2); n=20	Non-dominant 120.4 (47.8); n=18	11.0 [-15.2 to 37.2]	-0.27 [-0.91 to 0.37]	

CI = confidence intervals; ES = effect size; PTA = Percutaneous transluminal angioplasty; SD = standard deviation

Table 14. Mean change from baseline for Digit Span Test, CABG studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Vedin, 2006[3] / Randomized trial	6	CABG, off-pump	forward 7.4 (1.7); n=33	forward 7.2 (1.1); n=30	forward 0.20 [-0.50 to 0.90]	forward 0.14 [-0.36 to 0.63]	forward 0.17 [-0.33 to 0.67]
	6	CABG, on-pump	forward 7.1 (2.3); n=37	forward 7.2 (1.8); n=32	forward -0.10 [-1.07 to 0.87]	forward -0.05 [-0.52 to 0.43]	
	6	CABG, off-pump	backward 6.2 (1.6); n=33	backward 6.7 (1.5); n=30	backward -0.50 [-1.27 to 0.27]	backward -0.32 [-0.82 to 0.18]	backward 0.07 [-0.43 to 0.57]
	6	CABG, on-pump	backward 5.6 (1.7); n=37	backward 6.2 (1.0); n=32	backward -0.60 [-1.25 to 0.05]	backward -0.42 [-0.90 to 0.06]	
Lund, 2005[4] / Randomized trial	12	CABG, off-pump	9.8 (1.4); n=54	9.9 (1.6); n=54	-0.10 [-0.67 to 0.47]	-0.07 [-0.44 to 0.31]	0.13 [-0.25 to 0.51]
	12	CABG, on-pump	10.4 (2.0); n=52	10.8 (3.5); n=52	-0.40 [-1.50 to 0.70]	-0.14 [-0.52 to 0.25]	
Anastasiadis 2011[10] / Randomized trial	3	CABG with MECC	forward 6.5 (1.5); n=29	forward 6.9 (1.8); n=29	forward -0.40 [-1.25 to 0.45]	forward -0.24 [-0.75 to 0.28]	forward -0.46 [-0.98 to 0.05]
	3	CABG with CECC	forward 6.7 (2.1); n=31	forward 6.3 (1.5); n=31	forward 0.40 [-0.51 to 1.31]	forward 0.22 [-0.28 to 0.72]	
	3	CABG with MECC	backward 4.3 (1.6); n=29	backward 4.7 (1.4); n=29	backward -0.40 [-1.17 to 0.37]	backward -0.26 [-0.78 to 0.25]	backward -0.76 [-1.28 to -0.23]
	3	CABG with CECC	backward 4.1 (1.5); n=31	backward 3.5 (1.0); n=31	backward 0.60 [-0.03 to 1.23]	backward 0.46 [-0.04 to 0.97]	
Djaiani 2012[9] / Randomized trial	12	CABG with cell-saver	forward 10.1 (2.4); n=83	forward 10.1 (1.4); n=83	forward 0.00 [-0.60 to 0.60]	forward 0.00 [-0.30 to 0.30]	forward 0.15 [-0.15 to 0.46]
	12	CABG with suction	forward 10.2 (2.0); n=82	forward 10.5 (1.8); n=82	forward -0.30 [-0.88 to 0.28]	forward -0.16 [-0.46 to 0.15]	
	12	CABG with cell-saver	backward 6.3 (2.3); n=84	backward 6.7 (2.5); n=84	backward -0.40 [-1.13 to 0.33]	backward -0.17 [-0.47 to 0.14]	backward -0.25 [-0.56 to 0.05]
		CABG	backward	backward	backward	backward	

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
	12	with suction	6.4 (2.5); n=85	6.2 (2.1); n=85	0.20 [-0.49 to 0.89]	0.09 [-0.21 to 0.39]	
Boodhwani, 2007[6] /		CABG,	forward		forward		forward
	3	hypothermic	9.7 (2.2); n=133	NR	0.3 (1.7); n=119	NA	0.00 [-0.26 to 0.26]
		CABG,	forward		forward		
Randomized trial	3	normothermic	9.6 (2.0); n=134	NR	0.3 (1.7); n=117	NA	
		CABG,	backward		backward	backward	backward
	3	hypothermic	6.1 (2.1); n=133	NR	0.5 (1.9); n=119		1.93 [1.62 to 2.24]
		CABG,	backward		backward	backward	
	3	normothermic	6.3 (2.1); n=134	NR	-0.3 (1.7); n=117		
Nathan 2001[7] /		CABG,	forward		forward		forward
	60	hypothermic	7.3 (2.5); n=65	NR	-0.3 (2.0); n=65	NA	0.17 [-0.17 to 0.51]
Randomized trial		CABG,	forward		forward		
	60	normothermic	8.2 (2.3); n=66	NR	-0.6 (1.5); n=66	NA	
		CABG,	backward		backward		backward
	60	hypothermic	6.2 (2.4); n=65	NR	-0.1 (1.9); n=65	NA	0.00 [-0.34 to 0.34]
		CABG,	backward		backward		
	60	normothermic	6.8 (2.7); n=66	NR	-0.1 (2.2); n=66	NA	
Alex, 2005[13] /		CABG,	forward	forward	forward	forward	forward
	4	atmos. air	9.9 (2.7); n=31	9.5 (2.6); n=31	0.40 [-0.92 to 1.72]	0.15 [-0.35 to 0.65]	0.28 [-0.22 to 0.77]
Randomized trial		CABG,	forward	forward	forward	forward	
	4	oxygen	8.9 (2.3); n=33	9.2 (2.5); n=33	-0.30 [-1.46 to 0.86]	-0.12 [-0.61 to 0.36]	
		CABG,	backward	backward	backward	backward	backward
	4	atmos. air	6.8 (2.5); n=31	6.3 (2.2); n=31	0.50 [-0.67 to 1.67]	0.21 [-0.29 to 0.71]	0.31 [-0.18 to 0.81]
		CABG,	backward	backward	backward	backward	
	4	oxygen	5.9 (2.1); n=33	6.1 (2.1); n=33	-0.20 [-1.21 to 0.81]	-0.09 [-0.58 to 0.39]	
Flesch, 2009[11] /		CABG,	forward	forward	forward	forward	forward
	3	cardesartan	48.8 (10.1); n=53	47.9 (9.2); n=43	0.90 [-2.97 to 4.77]	0.09 [-0.31 to 0.49]	0.17 [-0.25 to 0.59]
Randomized trial		CABG,	forward	forward	forward	forward	
	3	placebo	50.0 (11.0); n=53	50.8 (10.7); n=44	-0.80 [-5.13 to 3.53]	-0.07 [-0.47 to 0.33]	
		CABG,	backward	backward	backward	backward	backward
	3	cardesartan	47.0 (10.0); n=53	46.7 (8.5); n=43	0.30 [-3.40 to 4.00]	0.03 [-0.37 to 0.43]	-0.04 [-0.46 to 0.38]
		CABG,	backward	backward	backward	backward	
	3	placebo	47.8 (10.4); n=53	47.1 (10.0); n=44	0.70 [-3.37 to 4.77]	0.07 [-0.33 to 0.47]	
Gold, 1995[15] /		CABG,					
	6	low MAP	14.8 (3.9); n=124	NR	0.0 (3.1); n=113	NA	-0.13 [-0.39 to 0.13]
Randomized trial		CABG,					
	6	high MAP	14.2 (4.0); n=124	NR	0.4 (2.9); n=112	NA	
Kadoi, 2003[27] /		CABG,	forward	forward	forward	forward	forward
	6	propofol	7.6 (2.0); n=77	8.0 (2.2); n=77	-0.40 [-1.06 to 0.26]	-0.19 [-0.51 to 0.13]	-0.09 [-0.41 to 0.23]
Randomized trial		CABG,	forward	forward	forward	forward	
	6	fentanyl	7.5 (2.2); n=75	7.7 (2.4); n=75	-0.20 [-0.94 to 0.54]	-0.09 [-0.41 to 0.23]	

Appendix M. Mean change from baseline tables

CI = confidence intervals; ES = effect size; PO = prospective observational study; RCT = randomized controlled trial; MAP = mean arterial pressure (during bypass); NSC = non-surgical control

Table 15. Mean change from baseline for Digit Symbol Test, CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lamy, 2013[1] /		CABG,					
	12	off-pump	33.0 (17.8); n=989	NR	1.8 (13.2); n=522	NA	0.04 [-0.08 to 0.16]
Randomized trial		CABG,					
	12	on-pump	31.9 (18.0); n=986	NR	1.3 (12.3); n=528	NA	
Jensen 2008[2]/		CABG,					
	12	off-pump	21.4 (6.4); n=61	22.3 (6.4); n=47	-0.90 [-3.33 to1.53]	-0.14 [-0.52 to 0.24]	0.02 [-0.40 to 0.43]
Randomized trial		CABG,					
	12	on-pump	20.5 (5.6); n=59	21.5 (6.1); n=43	-1.00 [-3.32 to 1.32]	-0.17 [-0.56 to 0.22]	
Vedin, 2006[3]/		CABG,	Symbol A	Symbol A	Symbol A	Symbol A	Symbol A
	6	off-pump	5.6 (2.3); n=33	5.7 (1.4); n=30	-0.10 [-1.03 to 0.83]	-0.05 [-0.55 to 0.44]	0.47 [-0.04 to 0.97]
Randomized trial		CABG,	Symbol A	Symbol A	Symbol A	Symbol A	
	6	on-pump	5.0 (2.6); n=37	6.0 (1.6); n=32	-1.00 [-2.00 to 0.00]	-0.45 [-0.93 to 0.03]	
		CABG,	Free recall	Free recall	Free recall	Free recall	Free recall
	6	off-pump	7.4 (1.6); n=33	7.7 (0.9); n=30	-0.30 [-0.93 to 0.33]	-0.23 [-0.72 to 0.27]	0.16 [-0.34 to 0.66]
		CABG,	Free recall	Free recall	Free recall	Free recall	
	6	on-pump	7.1 (1.5); n=37	7.6 (0.9); n=32	-0.50 [-1.08 to 0.08]	-0.39 [-0.87 to 0.09]	
		CABG,	90 seconds	90 seconds	90 seconds	90 seconds	90 seconds
	6	off-pump	40 (9.9); n=33	42 (4.1); n=30	-2.00 [-5.68 to 1.68]	-0.26 [-0.75 to 0.24]	0.12 [-0.38 to 0.62]
		CABG,	90 seconds	90 seconds	90 seconds	90 seconds	
	6	on-pump	36 (10.6); n=37	39 (7.1); n=32	-3.00 [-7.21 to 1.21]	-0.32 [-0.80 to 0.15]	
Lund 2005[4]/		CABG,					
	12	off-pump	36.6 (8.9); n=60	38.5 (10.2); n=54	-1.90 [-5.43 to 1.63]	-0.20 [-0.57 to 0.17]	0.08 [-0.30 to 0.46]
Randomized trial		CABG,					
	12	on-pump	36.4 (9.6); n=60	39.1 (10.1); n=52	-2.70 [-6.33 to 0.93]	-0.27 [-0.64 to 0.10]	
Lee 2003[5]/		CABG,					
	12	off-pump	45.3 (17.0); n=30	43.7 (14.5); n=27	1.60 [-6.58 to 9.78]	0.10 [-0.42 to 0.62]	0.16 [-0.38 to 0.70]
Randomized trial		CABG,					
	12	on-pump	52.5 (17.0); n=30	53.8 (22.1); n=26	-1.30 [-11.62 to 9.02]	-0.07 [-0.59 to 0.45]	
Boodhwani 2007[6]/		CABG,					
	3	hypothermic	42.9 (9.4); n=133	NR	2.1 (5.3); n=119	NA	0.05 [-0.21 to 0.30]
Randomized trial		CABG,					
	3	normothermic	43.1 (9.7); n=134	NR	1.8 (6.7); n=117	NA	
Anastasiadis 2011[10]/	3	CABG with MECC	36.7 (15.9); n=29	43.2 (17.1); n=29	-6.50 [-15.00 to 2.00]	-0.39 [-0.91 to 0.13]	-0.71 [-1.23 to -0.19]

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Randomized trial	3	CABG with CECC	29.7 (17.2); n=31	24.2 (17.7); n=31	5.50 [-3.19 to 14.19]	0.31 [-0.19 to 0.81]	
Gold, 1995[15] / Randomized trial	6	CABG, low MAP	40.9 (13.7); n=124	NR	2.5 (5.9); n=113	NA	-0.19 [-0.45 to 0.07]
	6	CABG, high MAP	41.4 (10.7); n=124	NR	3.7 (6.7); n=112	NA	
Silbert, 2006[12] / Randomized trial	12	CABG, low-dose fentanyl	34.8 (9.7); n=168	38.9 (10.9); n=159	-4.10 [-6.34 to -1.86]	-0.40 [-0.62 to -0.18]	-0.07 [-0.29 to 0.16]
	12	CABG, high-dose fentanyl	33.7 (10.3); n=158	37.1 (10.9); n=141	-3.40 [-5.81 to -0.99]	-0.32 [-0.55 to -0.09]	

CI = confidence intervals; ES = effect size; PO = prospective observational study; RCT = randomized controlled trial; MAP = mean arterial pressure (during bypass); NSC = non-surgical control

Table 16. Mean change from baseline for <u>Block Design (raw score)</u>, CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lund 2005[4] / Randomized trial	12	CABG, off-pump	26.4 (8.5); n=60	27.4 (9.7); n=54	-1.00 [-4.36 to 2.36]	-0.11 [-0.48 to 0.26]	0.01 [-0.37 to 0.39]
	12	CABG, on-pump	26.7 (9.2); n=60	27.8 (9.6); n=52	-1.10 [-4.60 to 2.40]	-0.12 [-0.49 to 0.26]	
Selnes, 2009[20] / Prospective observational	12	CABG, off-pump	22.9 (9.2); n=69	26.0 (9.6); n=54	-3.10 [-6.46 to 0.26]	-0.33 [-0.69 to 0.03]	Off vs. On -0.01 [-0.33 to 0.31]
	12	CABG, on-pump	23.2 (10.0); n=150	26.2 (10.2); n=123	-3.00 [-5.41 to -0.59]	-0.30 [-0.54 to -0.06]	Off vs. NSC -0.22 [-0.56 to 0.12]
	12	Non-surgical control	23.2 (9.5); n=99	24.2 (9.6); n=91	-1.00 [-3.72 to 1.72]	-0.10 [-0.39 to 0.18]	On vs. NSC -0.20 [-0.48 to 0.07]
	72	CABG, off-pump	22.9 (9.2); n=69	25.0 (10.3); n=43	-2.10 [-5.87 to 1.67]	-0.22 [-0.60 to 0.17]	Off vs. On -0.20 [-0.56 to 0.16]
	72	CABG, on-pump	23.2 (10.0); n=150	23.3 (10.2); n=93	-0.10 [-2.72 to 2.52]	-0.01 [-0.27 to 0.25]	Off vs. NSC -0.21 [-0.59 to 0.18]
	72	Non-surgical control	23.2 (9.5); n=99	23.3 (9.8); n=66	-0.10 [-3.12 to 2.92]	-0.01 [-0.32 to 0.30]	On vs. NSC 0.00 [-0.32 to 0.32]

CI = confidence intervals; ES = effect size

Appendix M. Mean change from baseline tables

Table 17. Mean change from baseline for Boston Naming Test or Vocabulary WAIS III, CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lee 2003[5] / (Vocabulary WAIS III)	12	CABG, off-pump	32.0 (13.8); n=30	29.7 (13.4); n=27	2.30 [-4.77 to 9.37]	0.17 [-0.35 to 0.69]	0.30 [-0.24 to 0.85]
Randomized trial	12	CABG, on-pump	38.0 (14.5); n=30	39.9 (14.2); n=26	-1.90 [-9.43 to 5.63]	-0.13 [-0.66 to 0.40]	
Selnes, 2009[20] / (Boston Naming Test)	12	CABG, off-pump	26.0 (3.7); n=71	26.5 (3.7); n=55	-0.50 [-1.80 to 0.80]	-0.13 [-0.49 to 0.22]	Off vs. On 0.12 [-0.20 to 0.44]
	12	CABG, on-pump	26.2 (3.7); n=152	27.1 (2.9); n=124	-0.90 [-1.68 to -0.12]	-0.27 [-0.50 to -0.03]	Off vs. NSC 0.03 [-0.31 to 0.36]
Prospective observational	12	Non-surgical control	26.1 (3.6); n=99	26.7 (3.3); n=91	-0.60 [-1.58 to 0.38]	-0.17 [-0.46 to 0.11]	On vs. NSC -0.09 [-0.36 to 0.18]
	72	CABG, off-pump	26.0 (3.7); n=71	26.3 (3.7); n=43	-0.30 [-1.70 to 1.10]	-0.08 [-0.46 to 0.30]	Off vs. On -0.16 [-0.52 to 0.21]
	72	CABG, on-pump	26.2 (3.7); n=152	25.9 (4.0); n=95	0.30 [-0.70 to 1.30]	0.08 [-0.18 to 0.33]	Off vs. NSC 0.03 [-0.35 to 0.41]
	72	Non-surgical control	26.1 (3.6); n=99	26.5 (3.0); n=67	-0.40 [-1.41 to 0.61]	-0.12 [-0.43 to 0.19]	On vs. NSC 0.19 [-0.12 to 0.51]
Gold 1995[15] / (Boston Naming Test)	6	CABG, low MAP	24.6 (4.4); n=124	NR	0.4 (2.0); n=113	NA	-0.19 [-0.45 to 0.08]
	6	CABG, high MAP	24.6 (4.6); n=124	NR	0.8 (2.3); n=112	NA	
Randomized trial							

CI = confidence intervals; ES = effect size; MAP = mean arterial pressure (during bypass); NSC = non-surgical control; WAIS = Wechsler Adult Intelligence Scale

Table 18. Mean change from baseline for Mini Mental State Exam, CABG studies. *Higher scores indicate a better result.*

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Kadoi 2003[27] /	6	CABG, propofol	46.4 (5.6); n=77	45.0 (5.9); n=77	-1.40 [-3.22 to 0.42]	0.24 [-0.07 to 0.56]	-0.03 [-0.35 to 0.28]
Randomized trial	6	CABG, fentanyl	47.7 (5.7); n=75	45.0 (6.4); n=75	-2.70 [-4.64 to -0.76]	0.44 [0.12 to 0.77]	
Selnes 2009[20] /	72	CABG, off-pump	27.7 (2.0); n=75	28.5 (1.8); n=43	-0.40 (1.6); n=43	-	Off vs. On -0.13 [-0.51 to 0.26]
		CABG,				-	Off vs. NSC

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Prospective observational	72	on-pump	27.6 (2.4); n=152	27.4 (2.5); n=96	-0.22 (2.0); n=96		-0.09 [-0.45 to 0.26]
	72	Non-surgical control	27.9 (2.0); n=99	28.0 (2.3); n=67	-0.12 (2.5); n=67	-	On vs. NSC -0.04 [-0.36 to 0.27]

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

Table 19. Mean change from baseline for Montreal Cognitive Assessment, CABG studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Lamy 2013[1] / Randomized trial	12	CABG, off-pump	23.2 (4.4); n=1053	NR	0.4 (4.0); n=645	NA	0.02 [-0.08 to 0.13]
	12	CABG, on-pump	23.2 (4.3); n=1028	NR	0.3 (4.0); n=628	NA	
Nathan 2001 [7] / Randomized trial	3	CABG, hypothermic	NR	NR	NR	NA	No focal deficits were discovered in either group at any examination.
	3	CABG, normothermic	NR	NR	NR	NA	

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

Table 20. Mean change from baseline for Mini Mental State Exam, CEA studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Baracchini 2012 [22] / Prospective observational	3	CEA Group A, symptomatic	27.4 (0.9); n=75	27.8 (0.9); n=75	0.40 [0.11 to 0.69]	-0.44 [-0.77 to -0.12]	Group A vs. Lap. 0.39 [0.06 to 0.72]
	3	CEA Group B, asymptomatic	27.8 (1.0); n=70	28.0 (1.1); n=70	0.20 [-0.15 to 0.55]	-0.19 [-0.52 to 0.14]	Group B vs. Lap. 0.22 [-0.12 to 0.55]
	3	. Laparoscopic Cholecystectomy	28.2 (1.5); n=68	28.1 (1.7); n=68	-0.10 [-0.64 to 0.44]	0.06 [-0.27 to 0.40]	Group A vs. B 0.20 [-0.13 to 0.53]
	12	CEA Group A, symptomatic	27.4 (0.9); n=75	27.7 (0.8); n=75	0.30 [0.03 to 0.57]	-0.35 [-0.67 to -0.03]	Group A vs. Lap. 0.26 [-0.07 to 0.59]
	12	CEA Group B, asymptomatic	27.8 (1.0); n=70	28.0 (1.1); n=70	0.20 [-0.15 to 0.55]	-0.19 [-0.52 to 0.14]	Group B vs. Lap. 0.16 [-0.17 to 0.50]

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
							Group A vs. B
	12	. Laparoscopic Cholecystectomy	28.2 (1.5); n=68	28.2 (1.2); n=68	0.00 [-0.46 to 0.46]	0.00 [-0.34 to 0.34]	0.10 [-0.22 to 0.43]

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

Table 21. Mean change from baseline for the Montreal Cognitive Assessment, CEA studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Baracchini 2012 [22] /							Group A vs. Lap.
	3	CEA Group A, symptomatic	26.0 (2.0); n=75	26.9 (1.7); n=75	0.90 [0.31 to 1.49]	-0.48 [-0.81 to -0.16]	0.52 [0.19 to 0.85]
		CEA Group B,					Group B vs. Lap.
Prospective observational	3	asymptomatic	26.8 (1.7); n=70	27.1 (1.3); n=70	0.30 [-0.20 to 0.80]	-0.20 [-0.53 to 0.13]	0.20 [-0.14 to 0.53]
		. Laparoscopic					Group A vs. B
	3	Cholecystectomy	27.1 (1.4); n=68	27.1 (1.7); n=68	0.00 [-0.52 to 0.52]	0.00 [-0.34 to 0.34]	0.35 [0.02 to 0.68]
		CEA Group A,					Group A vs. Lap.
	12	symptomatic	26.0 (2.0); n=75	27.0 (1.1); n=75	1.00 [0.48 to 1.52]	-0.62 [-0.94 to -0.29]	0.58 [0.24 to 0.91]
		CEA Group B,					Group B vs. Lap.
	12	asymptomatic	26.8 (1.7); n=70	27.2 (1.8); n=70	0.40 [-0.18 to 0.98]	-0.23 [-0.56 to 0.11]	0.19 [-0.15 to 0.52]
		. Laparoscopic					Group A vs. B
	12	Cholecystectomy	27.1 (1.4); n=68	27.2 (1.5); n=68	0.10 [-0.39 to 0.59]	-0.07 [-0.40 to 0.27]	0.36 [0.03 to 0.69]

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

Table 22. Mean change from baseline for Mini Mental State Exam, AVR studies. ***Higher scores indicate a better result.***

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
Fakin 2011[18] /							"Both patient groups scored normal throughout the whole study period (ranging from 29 to 30 points). This indicated that all patients were without an overt clinically relevant cognitive impairment at all points of
		AVR,					
Randomized trial	4	hypothermic	NR, "normal"	NR	NR		
		AVR,					
	4	normothermic	NR, "normal"	NR	NR		

Appendix M. Mean change from baseline tables

Study / Design	Follow-up (mos)	Intervention	Score at Baseline (SD); n	Score at Followup (SD); n	*Mean change from baseline (SD); n or [95%CI]*	ES [95%CI] within groups	ES [95%CI] between groups
							measurement."

CI = confidence intervals; COWAT = Controlled Oral Word Association Test; ES = effect size; NSC = non-surgical control; SD = standard deviation

* "Both patient groups scored normal throughout the whole study period (ranging from 29 to 30 points). This indicated that all patients were without an overt clinically relevant cognitive impairment at all points of measurement."

Table 23. Mean change from baseline for <u>domains from Altinbas 2011</u>: CAS versus CEA.

Study / Design	Follow-up (mos)	Domain	*Mean change from baseline z score (SD); n CAS*	*Mean change from baseline z score (SD); n CEA*	Mean difference [95%CI] between groups
Altinbas, 2011[16] / Randomized trial	6	Attention	-0.09 (1.05); n=59	-0.13 (1.60); n=57	0.04 [-0.46 to 0.53]
	6	Executive	0.13 (0.36); n=55	0.17 (0.48); n=45	-0.05 [-0.21 to 0.12]
	6	Language	-0.25 (0.68); n=59	-0.18 (0.70); n=58	-0.07 [-0.32 to 0.18]
	6	Verbal memory	-0.16 (0.76); n=59	-0.09 (1.00); n=56	-0.07 [-0.39 to 0.26]
	6	Visual memory	0.24 (0.72); n=53	0.24 (0.66); n=52	0.00 [-0.27 to 0.26]
	6	Visual perception	-0.14 (0.54); n=54	-0.17 (0.73); n=50	0.04 [-0.21 to 0.28]

CI = confidence intervals; ES = effect size; SD = standard deviation;

References

1. Lamy A, Devereaux PJ, Prabhakaran D, et al. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. N Engl J Med. 2013 Mar 28;368(13):1179-88. PMID: 23477676.
2. Jensen BO, Rasmussen LS, Steinbruchel DA. Cognitive outcomes in elderly high-risk patients 1 year after off-pump versus on-pump coronary artery bypass grafting. A randomized trial. Eur J Cardiothorac Surg. 2008 Nov;34(5):1016-21. PMID: 18778948.
3. Vedin J, Nyman H, Ericsson A, et al. Cognitive function after on or off pump coronary artery bypass grafting. Eur J Cardiothorac Surg. 2006 Aug;30(2):305-10. PMID: 16828295.
4. Lund C, Sundet K, Tennoe B, et al. Cerebral ischemic injury and cognitive impairment after off-pump and on-pump coronary artery bypass grafting surgery. Ann Thorac Surg. 2005 Dec;80(6):2126-31. PMID: 16305857.
5. Lee JD, Lee SJ, Tsushima WT, et al. Benefits of off-pump bypass on neurologic and clinical morbidity: a prospective randomized trial. Ann Thorac Surg. 2003 Jul;76(1):18-25; discussion -6. PMID: 12842506.
6. Boodhwani M, Rubens F, Wozny D, et al. Effects of sustained mild hypothermia on neurocognitive function after coronary artery bypass surgery: a randomized, double-blind study. J Thorac Cardiovasc Surg. 2007 Dec;134(6):1443-50; discussion 51-2. PMID: 18023662.
7. Nathan HJ, Wells GA, Munson JL, et al. Neuroprotective effect of mild hypothermia in patients undergoing coronary artery surgery with cardiopulmonary bypass: a randomized trial. Circulation. 2001 Sep 18;104(12 Suppl 1):I85-91. PMID: 11568036.
8. Nathan HJ, Rodriguez R, Wozny D, et al. Neuroprotective effect of mild hypothermia in patients undergoing coronary artery surgery with cardiopulmonary bypass: five-year follow-up of a randomized trial. J Thorac Cardiovasc Surg. 2007 May;133(5):1206-11. PMID: 17467430.
9. Djaiani G, Katznelson R, Fedorko L, et al. Early benefit of preserved cognitive function is not sustained at one-year after cardiac surgery: a longitudinal follow-up of the randomized controlled trial. Can J Anaesth. 2012 May;59(5):449-55. PMID: 22290354.
10. Anastasiadis K, Antonitsis P, Papakonstantinou C. When is the optimal time to perform neurocognitive assessment after coronary artery bypass surgery? Ann Thorac Surg. 2011 Nov;92(5):1933; author reply -4. PMID: 22051305.
11. Flesch M, Knipp S, Kessler G, et al. ARTA: AT1-receptor blocker therapy in patients undergoing coronary artery bypass grafting. Clin Res Cardiol. 2009 Jan;98(1):33-43. PMID: 18853093.
12. Silbert BS, Scott DA, Evered LA, et al. A comparison of the effect of high- and low-dose fentanyl on the incidence of postoperative cognitive dysfunction after coronary artery bypass surgery in the elderly. Anesthesiology. 2006 Jun;104(6):1137-45. PMID: 16732083.
13. Alex J, Laden G, Cale AR, et al. Pretreatment with hyperbaric oxygen and its effect on neuropsychometric dysfunction and systemic inflammatory response after cardiopulmonary bypass: a prospective randomized double-blind trial. J Thorac Cardiovasc Surg. 2005 Dec;130(6):1623-30. PMID: 16308008.
14. Kadoi Y, Kawauchi C, Ide M, et al. Preoperative depression is a risk factor for postoperative short-term and long-term cognitive dysfunction in patients with diabetes mellitus. J Anesth. 2011 Feb;25(1):10-7. PMID: 21161290.
15. Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. J Thorac Cardiovasc Surg. 1995 Nov;110(5):1302-11; discussion 11-4. PMID: 7475182.
16. Altinbas A, van Zandvoort MJ, van den Berg E, et al. Cognition after carotid endarterectomy or stenting: a randomized comparison. Neurology. 2011 Sep 13;77(11):1084-90. PMID: 21880992.
17. Crawley F, Stygall J, Lunn S, et al. Comparison of microembolism detected by transcranial Doppler and neuropsychological sequelae of carotid surgery and percutaneous transluminal angioplasty. Stroke. 2000 Jun;31(6):1329-34. PMID: 10835452.
18. Fakin R, Zimpfer D, Sodeck GH, et al. Influence of temperature management on neurocognitive function in biological aortic valve replacement. A prospective randomized trial. J Cardiovasc Surg (Torino). 2012 Feb;53(1):107-12. PMID: 22231536.
19. McKhann GM, Selnes OA, Grega MA, et al. Subjective memory symptoms in surgical and nonsurgical coronary artery patients: 6-year follow-up. Ann Thorac Surg. 2009 Jan;87(1):27-34. PMID: 19101263.
20. Selnes OA, Grega MA, Bailey MM, et al. Do management strategies for coronary artery disease influence 6-year cognitive outcomes? Ann Thorac Surg. 2009 Aug;88(2):445-54. PMID: 19632391.

21. Andrew MJ, Baker RA, Bennetts J, et al. A comparison of neuropsychologic deficits after extracardiac and intracaradiac surgery. J Cardiothorac Vasc Anesth. 2001 Feb;15(1):9-14. PMID: 11254832.
22. Baracchini C, Mazzalai F, Gruppo M, et al. Carotid endarterectomy protects elderly patients from cognitive decline: a prospective study. Surgery. 2012 Jan;151(1):99-106. PMID: 21943640.
23. Knipp SC, Kahlert P, Jokisch D, et al. Cognitive function after transapical aortic valve implantation: a single-centre study with 3-month follow-up. Interact Cardiovasc Thorac Surg. 2013 Feb;16(2):116-22. PMID: 23148084.
24. Jensen BO, Hughes P, Rasmussen LS, et al. Cognitive outcomes in elderly high-risk patients after off-pump versus conventional coronary artery bypass grafting: a randomized trial. Circulation. 2006 Jun 20;113(24):2790-5. PMID: 16769915.
25. Selnes OA, Zeger SL. Coronary artery bypass grafting baseline cognitive assessment: essential not optional. Ann Thorac Surg. 2007 Feb;83(2):374-6. PMID: 17257951.
26. Selnes OA, Grega MA, Borowicz LM, Jr., et al. Cognitive outcomes three years after coronary artery bypass surgery: a comparison of on-pump coronary artery bypass graft surgery and nonsurgical controls. Ann Thorac Surg. 2005 Apr;79(4):1201-9. PMID: 15797050.
27. Kadoi Y, Saito S, Kunimoto F, et al. Comparative effects of propofol versus fentanyl on cerebral oxygenation state during normothermic cardiopulmonary bypass and postoperative cognitive dysfunction. Annals of Thoracic Surgery. 2003 Mar;75(3):840-6. PMID: 12645704.
28. McKhann GM, Grega MA, Borowicz LM, Jr., et al. Is there cognitive decline 1 year after CABG? Comparison with surgical and nonsurgical controls. Neurology. 2005 Oct 11;65(7):991-9. PMID: 16107605.