# **SYSTEMATIC REVIEW AND META-ANALYSIS**

# Risk Factors for Delirium and Cognitive Decline Following Coronary Artery Bypass Grafting Surgery: A Systematic Review and Meta-Analysis

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**BACKGROUND:** Coronary artery bypass grafting (CABG) is known to improve heart function and quality of life, while rates of surgery-related mortality are low. However, delirium and cognitive decline are common complications. We sought to identify preoperative, intraoperative, and postoperative risk or protective factors associated with delirium and cognitive decline (across time) in patients undergoing CABG.

**METHODS AND RESULTS:** We conducted a systematic search of Medline, PsycINFO, EMBASE, and Cochrane (March 26, 2019) for peer-reviewed, English publications reporting post-CABG delirium or cognitive decline data, for at least one risk factor. Random-effects meta-analyses estimated pooled odds ratio for categorical data and mean difference or standardized mean difference for continuous data. Ninety-seven studies, comprising data from 60 479 patients who underwent CABG, were included. Moderate to large and statistically significant risk factors for delirium were as follows: (1) preoperative cognitive impairment, depression, stroke history, and higher European System for Cardiac Operative Risk Evaluation (EuroSCORE) score, (2) intraoperative increase in intubation time, and (3) postoperative presence of arrythmia and increased days in the intensive care unit; higher preoperative cognitive performance was protective for delirium. Moderate to large and statistically significant risk factors for acute cognitive decline were as follows: (1) preoperative depression and older age, (2) intraoperative increase in intubation time, and (3) postoperative depression and older age, (2) intraoperative increase in intubation time, and increased days in the intensive care unit. Presence of depression preoperative yas a moderate risk factor for midterm (1–6 months) post-CABG cognitive decline.

**CONCLUSIONS:** This meta-analysis identified several key risk factors for delirium and cognitive decline following CABG, most of which are nonmodifiable. Future research should target preoperative risk factors, such as depression or cognitive impairment, which are potentially modifiable.

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**C** oronary artery bypass grafting (CABG) surgery is the main treatment for multivessel coronary disease and remains one of the most common cardiac procedures worldwide.<sup>1,2</sup> CABG has low mortality rates, and improves coronary vascularization and cardiac function.<sup>3</sup> However, CABG is associated with high rates of postoperative cognitive impairments, including delirium.  $^{\rm 4-6}$ 

A recent meta-analysis investigating post-CABG cognitive outcomes (cross-sectional approach by percentage at specific time points)<sup>4</sup> revealed postoperative cognitive impairment or decline was prevalent in

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# **CLINICAL PERSPECTIVE**

#### What Is New?

- This meta-analysis is the first to comprehensively identify risk and protective factors for postoperative delirium and cognitive decline in patients who underwent coronary artery bypass grafting (CABG).
- Findings demonstrate that there are many risk and protective factors for delirium and cognitive decline post-CABG, some of which are modifiable, such as depression, diabetes mellitus, hypertension, and cognitive impairment.
- The presence of preoperative depression was a common risk factor across outcomes, which at least doubled the risk of post-CABG delirium in hospital and cognitive decline acutely and up to 6 months following surgery.

# What Are the Clinical Implications?

- Risk and protective factors identified in this meta-analysis could be used to improve delirium and cognitive decline risk prediction tools, leading to more accurate identification of at-risk patients undergoing CABG, improving care and prognosis.
- Findings can inform the design of future intervention trials aimed at reducing the incidence of delirium and cognitive decline post-CABG, by targeting identified modifiable risk factors.

# Nonstandard Abbreviations and Acronyms

ACC aortic cross-clamp CPB cardiopulmonary bypass

- SMD standardized mean difference
- 43% of patients up to 4 days, and remains high (39%) up to 1 month post-CABG. This reduces in the midterm (6–12 months) following CABG to  $\approx$ 25% and increases up to nearly 40% in the long-term (1–5 years). The presence of delirium (an acute and fluctuating syndrome of deficits in attention and arousal) was apparent in 24% of patients, up to 1 week post-CABG, when a standardized tool was used alongside clinical criteria.<sup>4</sup>

The presence of cognitive decline following CABG is associated with increased depression risk and decreased quality of life, functional capacity, and the ability to perform activities of daily living.<sup>7</sup> Delirium presence in older adults is associated with increased mortality, length of stay (LOS), hospital readmissions, as well as cognitive decline and dementia, along with reduced quality of life.<sup>8–11</sup> Research attempting to

prevent these post-CABG cognitive outcomes has been largely unsuccessful, including pharmacological, anesthetic intervention, and surgical techniques.<sup>12–16</sup> There has been some evidence of therapeutic effect for advanced surgical methods, such as hypothermia and increasing systemic perfusion intraoperatively.<sup>17</sup> However, the expertise and technology needed are not routinely available.

Understanding risk and protective factors for delirium and cognitive decline post-CABG has critical clinical implications, including more precise targeting of preoperative and perioperative interventions and the development of a sensitive risk screening tool for these outcomes. The use of a prediction tool for delirium and cognitive decline in a post-CABG setting could lead to earlier intervention opportunities, greater prognosis, and, in turn, better patient management.

Previous meta-analyses of all surgical type cardiac patients have provided greater depth of knowledge surrounding the effects of surgery method on cognitive decline (on versus off pump)<sup>15,16</sup> and the effect of pharmacological and anesthetic interventions on postoperative delirium.<sup>18,19</sup> Specific risk or protective factors for cognitive outcomes (delirium and cognitive decline) have not been comprehensively investigated through meta-analysis in patients undergoing CABG. In addition, no meta-analysis has investigated the time course of effects for risk factors in relation to cognitive decline following CABG, especially in the long-term (>12 months). This systematic review and meta-analysis aims to investigate risk and protective factors for the following: (1) post-CABG delirium (1-7 days) and (2) post-CABG cognitive decline across multiple time points: short-term (immediately postoperatively up to 1 month), midterm (1-6 months postoperatively), and long-term (12-15 months postoperatively).

# **METHODS**

The protocol for this systematic review and metaanalysis was registered and published with the international prospective register of systematic reviews (PROSPERO) (registration number: CRD42020149276). This article is reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.<sup>20</sup> The data that support the findings of this study are available from the corresponding author on reasonable request.

### **Search Strategy**

We updated a search from a published meta-analysis.<sup>4</sup> We searched Medline, PsycINFO, EMBASE, and the

Cochrane databases using the Ovid platform when possible. Searches of all databases were last performed on March 26, 2019. Search terms and medical subject headings used were as follows: (Coronary Artery Bypass/ OR "coronary artery bypass" OR CABG) AND (Cognition/ OR Delirium/ OR Dementia/ OR Alzheimer Disease/ OR Neuropsychological Tests/ OR Cognit\* OR Deliri\* OR Dementia\* OR Alzheimer\* MCI or "mild cognitive impairment\*" OR "mild-cognitive impairment\*" OR neuropsycholo\* OR POCD OR "postoperative cognitive" OR "post-operative cognitive" OR MMSE OR "mini-mental state examination" OR "cerebral function" OR neurocognit\* OR encephalopath\*). Article selection and data extraction, of the updated search, were undertaken by at least 2 reviewers (between D.G., E.S.G., and T.J.R.), with disagreements resolved by consensus.

# **Study Eligibility**

Inclusion criteria were as follows: peer-reviewed, full-text, English-language studies that reported usable risk or protective factor data of those who had undergone CABG surgery (including CABG plus concomitant surgeries). Studies needed to report a cognitive outcome (using a standardized test result, neuropsychological battery, or a clinical diagnosis) for presence of delirium versus no delirium or cognitive decline versus no cognitive decline, and include usable data for at least one risk factor.

Exclusion criteria included the following: case series (n<5), dissertations, book chapters, protocol articles, reviews, news articles, conference abstracts, letters to the editor, editorials, and comment publications; and studies with no description of their operationalization (or definition used for categorizing participants with cognitive decline/delirium) or incomplete reporting in respect to risk factor data.

All possible risk/protective factors were tallied for presence across eligible studies (eg, data reported within text or within a table split by cognitive outcome or results of measures of association, such as odds ratios [ORs]). Unique risk factors that were reported in >10 studies (across delirium and cognitive decline) were included in this review. A list of these factors was circulated to academic clinicians (coauthors P.J.P. and D.H.J.D.) to ensure that no clinically relevant factors had been missed. This led to the additional extraction of delirium as a risk factor for cognitive decline (although only present in 3 studies). Following this, factors were categorized as follows: preoperative, intraoperative, or postoperative. Studies that did not report information pertaining to the target risk factors analyzed within the study (eg, studies reporting data related to hematocrit, height, or sepsis) were subsequently excluded (categorized as inappropriate data). In addition, if multiple studies investigated the same cohort, duplicate samples were excluded.

#### **Quality Assessment**

Study design and reporting quality were assessed by at least 2 reviewers (between D.G., E.S.G., and T.J.R.), with disagreements resolved by consensus. An adapted tool was used, on the basis of 2 existing assessment checklists,<sup>21,22</sup> where higher scores indicated greater overall quality (0–12) (Data S1).

#### **Data Extraction**

Data extracted from each included study consisted of: country, sample size, age, sex, cognitive decline/delirium assessment criteria, and risk factor data relative to time periods and cognitive outcome (delirium versus no delirium): 1 to 7 days postoperatively; postoperative cognitive decline versus no decline: short-term (immediately postoperatively up to 1 month), midterm (1-6 months postoperatively), and long-term (12-15 months postoperatively). There may be a small degree of overlap between the outcomes of delirium and acute cognitive decline, yet this overlap is representative of the population at this time point. Many of the studies included in this meta-analysis did not explicitly aim to assess risk factors for these cognitive outcomes through inferential statistical analyses. Yet, these studies still reported extractable descriptive data related to the cognitive outcome (eg, table presenting counts or mean and SD for preoperative, intraoperative, and postoperative variables, split by cognitive outcome). As fewer articles reported data as a result of an inferential statistical analysis, the extraction of descriptive data was prioritized. For each risk factor, descriptive data (eg, mean and SD/event rates) were extracted when available. In the absence of descriptive data, the results of inferential statistical analyses (eg, ORs) were extracted. To increase the consistency within our analyses, only univariate (or unadjusted) data were extracted, as the number and type of covariates used within risk factor analyses varied greatly across studies. When data were reported and extracted as median and interguartile range values, they were converted to mean and SD values.<sup>23,24</sup> Only data pertaining to risk/ protective factors could be extracted for each cognitive outcome for the time periods reported in identified studies. There were substantially fewer articles within the literature that investigate midterm and long-term cognitive decline, compared with delirium and acute cognitive decline. Therefore, fewer risk factors could be investigated for midterm and long-term cognitive decline. It may be the case that there are important risk factors for these time points that we were unable to identify herein with our approach.

### **Statistical Analysis**

Demographic data were calculated from the reported preoperative samples. The  ${\sf I}^2$  statistic was used to

express the proportion of between-study heterogeneity out of total variance and was classified as low ( $l^2=25\%$ – 50%), moderate ( $l^2=50\%$ –75%), or high ( $l^2\ge75\%$ ), using classification criteria suggested by Higgins et al.<sup>25</sup> Total between-study variance was quantified using  $\tau^2$ . All analyses were based on random-effects model. Before data analyses, checks were conducted to detect extreme outliers. Effect size estimates that fell an abnormally large distance from other estimates (mainly because of separation or quasi-separation for a given outcome) were excluded. This process did not exclude the remaining study data from remaining risk factor analyses.

All analyses were performed in Comprehensive Meta-Analysis software (version 3). A result was considered statistically significant when P<0.05. Each risk or protective factor was analyzed separately and, therefore, independence from other factors cannot be assumed. Separate random effect meta-analyses were used to estimate pooled OR for categorical risk factor data and mean difference or standardized mean difference (SMD) for continuous risk factor data, comparing cognitive outcomes (delirium versus no delirium or cognitive decline versus no cognitive decline) post-CABG. A risk or protective factor was meta-analyzed when data from  $\geq 2$  studies were available for the analysis. All meta-analyses were conducted on univariate data (no multivariate data were extracted) and therefore should be interpreted as unadjusted pooled estimates. The SMD was also calculated to provide a supplementary common effect size across pooled estimates (Tables S1 through S4). SMD values can be interpreted using the same cutoff as Cohen d, where  $\geq 0.20$ ,  $\geq 0.50$ , and  $\geq 0.80$ are considered as small, moderate, and large, respectively.<sup>26</sup> For cognitive decline post-CABG, analvses were conducted for each time point: short-term (immediately postoperatively up to 1 month), midterm (1-6 months postoperatively), and long-term (12-15 months postoperatively). Some of the extracted predictor variables were presented as both categorical and continuous data across articles (eq. education >12 years [categorical] or total years of education [continuous]). Others provided data that could be sorted into multiple categories (eg, preoperative cognitive test scores): (1) different cognitive tests used between studies (SMD used) or (2) the same test used between studies, such as Mini-Mental State Examination (mean difference used). In these cases, subanalyses were performed for each data format or category, for each risk factor. For statistically significant results, small study effect was examined by visually inspecting funnel plots of effect size versus SE.<sup>27</sup> When at least 10 studies were available for analyses, small study effect was formally assessed using the Egger test of the intercept.<sup>28</sup> When there was evidence for small study effect (1-tailed P<0.1), we used the Duvall and Tweedie<sup>29</sup> trim and fill method to quantify the extent of potential bias. When there were <10 studies, we performed sensitivity analyses by removing outliers.

Random-effects meta-regressions (using mean age as a covariate within the analysis) were performed to investigate whether age was related to the pooled effect estimates. Only analyses containing both risk factor and age data of ≥10 studies, as stated in recent Cochrane guidelines,<sup>30</sup> were interpreted. We also performed stratified random-effects subgroup analyses to investigate any possible effects of diagnostic approach for delirium (inclusion of a standardized instrument versus none) for each risk factor. For this, stratified random-effects meta-analyses were performed for each risk or protective factor variable relative to (1) studies using a standardized instrument (eq. Confusion Assessment Method or the Delirium Rating Scale) to inform the reference standard and (2) studies not using a specific instrument. Therefore, 2 subgroup meta-analyses were conducted for each risk factor variable (1 of studies using a diagnostic tool and 1 of studies using no tool), allowing comparison of the pooled estimates. Subgroup analyses investigating differing methods of classifying cognitive decline were not conducted because of the limited numbers of articles across most time points.

# RESULTS

The search identified 4260 articles, of which 2647 records were screened by title and abstract, following duplicate removal. Full-text screening was conducted on 963 articles; of these, 97 were included in this review (Figure 1, see Table S5 for articles excluded and rationale for exclusion, at full-text review stage).

The 97 included studies were published across 4 decades, with 3, 7, 38, and 49 studies published in the 1980s, 1990s, 2000s, and 2010s, respectively. Of the included studies, 17 were conducted in the United States, 13 in Japan, 9 in Canada, 8 in Australia, and 6 each in China and the Netherlands. The remaining 38 studies were conducted across 22 individual countries. The included articles comprised data from 60 479 patients, with individual study sample sizes ranging from 8 to 14 262. The mean age of patients across included studies was 64.54 years, and 68.55% of patients were men (calculated only from studies with available data). The included studies were of good quality on the basis of the critical appraisals, ranging from 4 to 12, with a median study score of 10 (of 12) and interguartile range of 8 to 11.5. No studies were excluded from the analysis on the basis of their quality (see Table S6 for individual study information).

#### Greaves et al

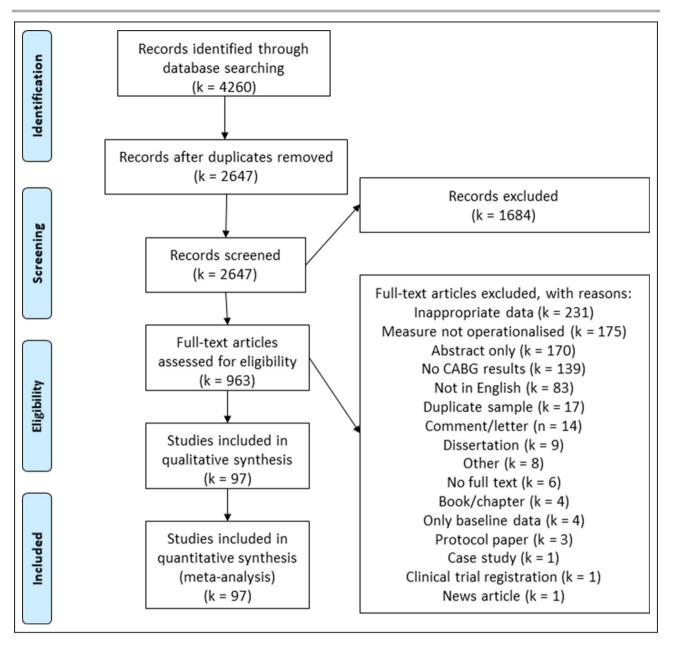


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram. CABG indicates coronary artery bypass grafting.

Preanalysis checks for extreme outliers resulted in data from 3 studies being excluded from separate analyses (delirium analyses of: presence of depression, kidney injury, and LOS in intensive care unit [ICU]); however, these studies remained within other analyses and therefore were not excluded from this article.

#### Delirium

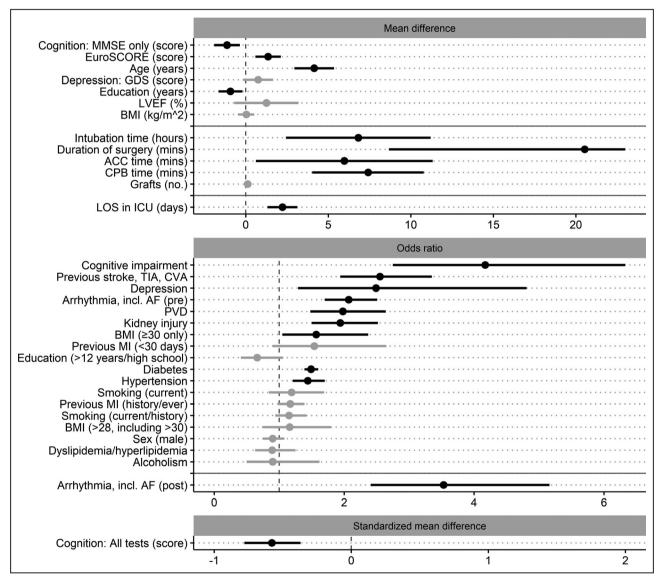
Data from 48 individual studies were used within 33 analyses (including subcategory analyses), investigating 27 separate risk or protective factors for delirium presence post-CABG. Across the analyses, heterogeneity of statistically significant results spanned from

low to high (I<sup>2</sup> range, 0–98.40;  $\tau^2$  range, 0–325.89) (see Table S1 for results of each meta-analysis and Figure S1 for forest plots). Potential small-study effect was found in 2 analyses (preoperative age and European System for Cardiac Operative Risk Evaluation (EuroSCORE)), where trim and fill estimation led to decreases in effect size (see Figure S2 for funnel plots and small study effect investigation).

Statistically significant preoperative risk factors of developing delirium post-CABG, from largest to smallest effect size, were: the presence of cognitive impairment, stroke history, depression, arrhythmia, including atrial fibrillation (AF), peripheral vascular disease, kidney injury/disease, body mass index >30 kg/m<sup>2</sup>, diabetes mellitus, and hypertension, along with continuous risk factors of higher EuroSCORE and older age. Statistically significant intraoperative risk factors, from largest to smallest effect size, were increased intubation time (hours), duration of surgery (minutes), aortic cross-clamp (ACC) time (minutes), and cardio-pulmonary bypass (CPB) time (minutes). Statistically significant postoperative risk factors, from largest to

smallest effect size, were: increased LOS in the ICU (days) and the presence of arrhythmia, including AF. Statistically significant protective factors for developing delirium post-CABG were higher preoperative cognition test scores and years of education (Table S1 and Figure 2).

Preoperative factors that did not reach statistical significance were: the presence of alcoholism, body mass index >28 kg/m<sup>2</sup>, dyslipidemia/hyperlipidemia,



**Figure 2.** Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting delirium. Factors grouped according to the primary pooled estimate of the analysis (mean difference [MD], odds ratio, or standardized MD [SMD]), where solid gray horizontal lines indicate separation of preoperative, intraoperative, and postoperative factors and dashed gray vertical lines divide protective (left side) and risk (right side) factor estimates. The pooled estimates are ordered by the common calculated effect size (SMD) from largest to smallest (largest at the top). Estimates that are black represent statistically significant factors; those that are gray did not reach statistical significance. The scale for all continuous variables (MD and SMD plots) is listed within each factor name. The CIs for duration of surgery extend further than the visible portion of the figure. This was not shown to allow appropriate visibility of all pooled estimates. ACC indicates aortic cross-clamp; AF, atrial fibrillation; BMI, body mass index; CPB, cardiopulmonary bypass; CVA, cerebrovascular attack; GDS, Geriatric Depression Scale; ICU, intensive care unit; LOS, length of stay; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MMSE, Mini-Mental State Examination; PVD, peripheral vascular disease; and TIA, transient ischemic attack. >12 years of education, male sex, previous myocardial infarction, and previous/current smoking; and continuous factors of higher body mass index, depression score, and left ventricular ejection fraction. With respect to intraoperative factors, number of grafts did not reach statistical significance (Table S1 and Figure 2).

Subgroup analyses investigating the effect of diagnostic criteria for delirium (studies using standardized measurement tool along with diagnostic criteria versus studies using no tool) revealed no meaningful differences for any risk factors, with CIs overlapping for all analyses (Table S7). Meta-regressions with mean age as a model factor (covariate) revealed statistically significant results for risk factors of ACC time (age:  $\beta = -1.33$ , Z=-2.49, P=0.013, R<sup>2</sup>=0.50) and LOS in ICU (age: β=-0.22, Z=-1.99, P=0.046,  $R^2$ =0.10). These results suggest that as the mean age of the study sample increases, the delirium risk associated with ACC time and LOS in ICU decreases. The results also suggest that 50% (for ACC time) and 10% (for LOS in ICU) of the variance in delirium presence relating to these risk factors can be attributed to age.

# Acute Cognitive Decline (Immediately to 1-Month Post-CABG)

Data from 35 individual studies were used within 30 analyses (including subcategory analyses), investigating 25 separate risk or protective factors for the presence of cognitive decline acutely (immediately up to 1 month) post-CABG. Across the analyses, heterogeneity of statistically significant results spanned from low to high (I<sup>2</sup> range, 0–92.85;  $\tau^2$  range, 0–32.28) (see Table S2 for results of each meta-analysis and Figure S3 for forest plots). Potential small study effect was found in 2 analyses. Trim and fill estimation for preoperative age led to a decrease in effect size (see Figure S4 for funnel plots and small study effect investigation). A sensitivity analysis was performed for postoperative delirium (removal of outlier), which resulted in a decrease in effect size (Table S2 and Figure 3).

Statistically significant preoperative risk factors for acute post-CABG cognitive decline, from largest to smallest effect size, were: the presence of depression, stroke history, hypertension, and diabetes mellitus, along with continuous risk factors of older age and higher EuroSCORE. Statistically significant intraoperative continuous risk factors, from largest to smallest effect size, were increased intubation time (hours) and duration of surgery (minutes). Statistically significant postoperative risk factors, from largest to smallest effect size, were: the presence of delirium and arrhythmia, including AF, and the continuous risk factor of increased LOS in the ICU (days). Higher body mass index was a statistically significant protective factor for acute post-CABG cognitive decline (Table S2 and Figure 3).

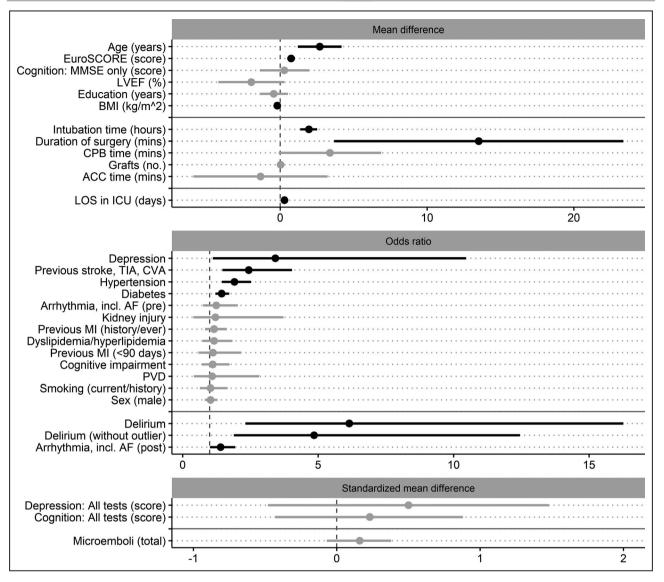
Preoperative factors that did not reach statistical significance were the presence of arrhythmia, including AF, cognitive impairment, dyslipidemia/hyperlipidemia, male sex, kidney injury/disease, previous myocardial infarction, peripheral vascular disease, and previous/current smoking; and continuous factors of higher cognitive test score, depression score, years of education, and lower left ventricular ejection fraction. Intraoperative factors that did not reach statistical significance were increase in ACC time (minutes), CPB time (minutes), number of grafts, and total microemboli count (Table S2 and Figure 3).

Meta-regressions revealed that 49% of the variance in acute cognitive decline for the risk factor of increased CPB time (age:  $\beta$ =-0.88, Z=-2.24, P=0.025, R<sup>2</sup>=0.49) can be attributed to age. These results suggest that as the mean age of the study sample increases, the risk of cognitive decline associated with CPB time decreases.

# Midterm Cognitive Decline (1–6 Months Post-CABG)

Data from 24 individual studies were used within 19 analyses (including subcategory analyses), investigating 17 separate risk or protective factors for the presence of cognitive decline in the midterm (1–6 months) post-CABG. Across the analyses, heterogeneity of statistically significant results spanned from low to moderate (l<sup>2</sup> range, 0–68.84;  $\tau^2$  range, 0–0.04) (see Table S3 for results of each meta-analysis and Figure S5 for forest plots). Two analyses revealed statistically significant results, with no indication of small study effect (Figure S6). Preoperative depression and higher cognitive test scores (across all tests) were risk factors for midterm post-CABG cognitive decline (Table S3 and Figure 4).

Preoperative factors that did not reach statistical significance were the presence of diabetes mellitus, male sex, hypertension, previous myocardial infarction, stroke history, peripheral vascular disease, and current smoking; and continuous factors of higher age, cognitive test score (when using cognitive index), depression score, years of education, and left ventricular ejection fraction. No intraoperative or postoperative factors reached statistical significance, including increase in ACC time (minutes), CPB time (minutes), number of grafts, total microemboli count, and LOS in ICU (days) (Table S3 and Figure 4). No meta-regressions investigating the influence of age were significant for this time point.



# Figure 3. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting acute cognitive decline.

Factors grouped according to the primary pooled estimate of the analysis (mean difference [MD], odds ratio, or standardized MD [SMD]), where solid gray horizontal lines indicate separation of preoperative, intraoperative, and postoperative factors and dashed gray vertical lines divide protective (left side) and risk (right side) factor estimates. The pooled estimates are ordered by the common calculated effect size (SMD) from largest to smallest (largest at the top). Estimates that are black represent statistically significant factors; those that are gray did not reach statistical significance. The scale for all continuous variables (MD and SMD plots) is listed within each factor name. ACC indicates aortic cross-clamp; AF, atrial fibrillation; BMI, body mass index; CPB, cardiopulmonary bypass; CVA, cerebrovascular attack; ICU, intensive care unit; LOS, length of stay; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MMSE, Mini-Mental State Examination; PVD, peripheral vascular disease; and TIA, transient ischemic attack.

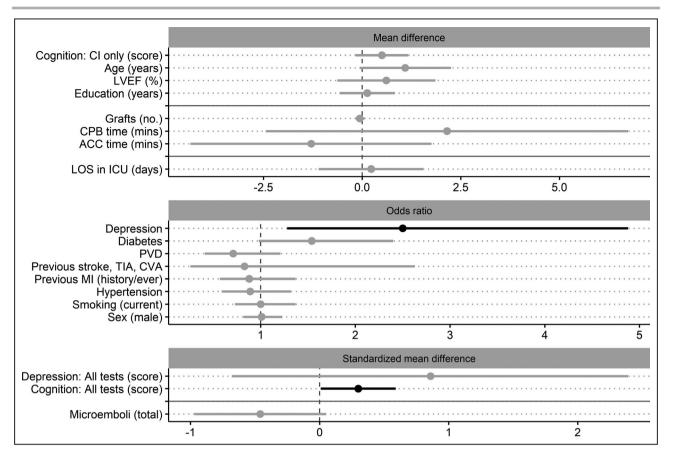
### Long-Term Cognitive Decline (12–15 Months Post-CABG)

Data from 5 individual studies were used within 6 separate risk factor analyses for cognitive decline in the long-term (12–15 months) post-CABG. No analyses revealed statistically significant results, including presence of preoperative cognitive impairment, diabetes mellitus, male sex, and hypertension, nor older age or higher number of intraoperative grafts (see Table S4 for results of each meta-analysis, Figure S7 for forest plots, and Figure 5). No meta-regressions were performed for this time point.

# DISCUSSION

This meta-analysis quantifies data from >60 000 patients to identify risk and protective factors for the development of cognitive decline, including delirium,





# Figure 4. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting midterm cognitive decline.

Factors grouped according to the primary pooled estimate of the analysis (mean difference [MD], odds ratio, or standardized MD [SMD]), where solid gray horizontal lines indicate separation of preoperative, intraoperative, and postoperative factors and dashed gray vertical lines divide protective (left side) and risk (right side) factor estimates. The pooled estimates are ordered by the common calculated effect size (SMD) from largest to smallest (largest at the top). Estimates that are black represent statistically significant factors; those that are gray did not reach statistical significance. The scale for all continuous variables (MD and SMD plots) is listed within each factor name. ACC indicates aortic cross-clamp; CI, cognitive index score; CPB, cardiopulmonary bypass; CVA, cerebrovascular attack; ICU, intensive care unit; LOS, length of stay; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PVD, peripheral vascular disease; and TIA, transient ischemic attack.

immediately following CABG and in the midterm and long-term. Findings highlight that there are many risk factors for both delirium and cognitive decline following CABG. These factors could be integrated into existing delirium tools or shortlisted in the development of prediction tools for postoperative cognitive decline.<sup>31,32</sup> Further development of these clinical risk screening tools for both delirium and cognitive decline post-CABG could lead to more accurate identification of at-risk patients, improved prognosis, targeting of interventions, and patient management.

Risk prediction for delirium has been discussed at length for nonsurgical patients, with current models generally thought to have inadequate accuracy.<sup>32</sup> Most published delirium prediction tools are based on individual clinical studies with low statistical power, decreasing their generalizability.<sup>33–36</sup> To our knowledge, no tools have been developed for predicting

postoperative cognitive decline, nor have they been developed for delirium specifically following CABG. The results of this meta-analysis can provide a shortlist of risk and protective factors that should be considered in future research for the modeling of prediction tools. Specifically, results should be considered when modifying or developing tools related to post-CABG cognitive outcomes, as the operative process differs from other surgeries (eg, the use of CPB). Similar risk and protective factors may be applicable to other surgery types (cardiac and noncardiac); however, these factors cannot be ascertained from the current meta-analysis. The development of CABG-specific tools (delirium and cognitive decline) may lead to better prognosis, because of earlier identification and risk reduction strategies.

Delirium has been said to be preventable in up to 40% of cases.<sup>9</sup> Recent editorials<sup>37,38</sup> have highlighted

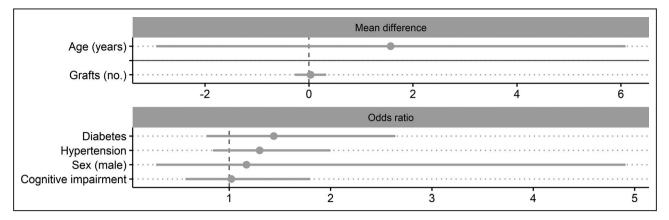


Figure 5. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting long-term cognitive decline.

Factors grouped according to the primary pooled estimate of the analysis (mean difference [MD], odds ratio, or standardized MD [SMD]), where solid gray horizontal lines indicate separation of preoperative, intraoperative, and postoperative factors and dashed gray vertical lines divide protective (left side) and risk (right side) factor estimates. The pooled estimates are ordered by the common calculated effect size (SMD) from largest to smallest (largest at the top). Estimates that are black represent statistically significant factors; those that are gray did not reach statistical significance. The scale for all continuous variables (MD and SMD plots) is listed within each factor name.

the importance of decreasing the incidence of delirium and cognitive decline to decrease patient and economic burden. In this meta-analysis, modifiable risk factors, such as the presence of preoperative depression, diabetes mellitus, and hypertension, were found to increase the risk (ORs, 1.44-3.42) for both delirium and cognitive decline acutely post-CABG. Future research should investigate the effectiveness of implementing preoperative management strategies of these factors on cognitive outcomes (delirium and cognitive decline) post-CABG. The presence of cognitive impairment resulted in over a 4-fold increase in risk of developing post-CABG delirium. Cognition is known to be modifiable through cognitive training in older populations, including those presenting with heart failure, 39-41 and therefore may be a viable preoperative target of intervention.<sup>42</sup>

In this meta-analysis, preoperative depression moderately (moderate effect sizes) increased the risk of delirium (OR, 2.49), acute cognitive decline (OR, 3.42), and midterm cognitive decline (OR, 2.50) post-CABG. In addition, a higher preoperative depression score revealed moderate to large (SMD, 0.50-0.86) increases in the risk of developing acute and midterm cognitive decline post-CABG, yet these analyses were not statistically significant, possibly because of high heterogeneity (l<sup>2</sup>, 93.32–96.08; τ<sup>2</sup>, 0.92–1.75). Depression in late life is known to occur concurrently with cognitive impairment and can hasten the onset of dementia.43 The presence of vascular disease (indicative of undergoing CABG) is considered to have a strong link to the development of depression and dementia.<sup>44</sup> Therefore, the effects seen across the meta-analyses in relation to depression may not be independent from other factors. We endeavored to investigate the influence of these factors through meta-regression, yet it was not possible because of limited studies concurrently reporting data relating to depression, cognitive impairment, and vascular disease (eg, peripheral vascular disease, hypertension, and dyslipidemia).

The presence of delirium following CABG resulted in a near 5-fold increase (OR, 4.85, following sensitivity analysis) in risk of acute post-CABG cognitive decline (up to 1 month). This pooled effect size was not adjusted for any preoperative or intraoperative risk factors and, therefore, its independence cannot be assumed and should be interpreted with this in mind. It may be argued that in a short-term setting, this risk can be inflated because of the cognitive deficits of the delirium episode itself. However, the presence of delirium at this time (acute cognitive decline) is unlikely, as the assessment period for the 3 included studies was between days 7 and 9, whereas we know delirium typically resolves by day 5.45-47 No studies reported data related to associations between post-CABG delirium and cognitive decline in the midterm and long-term. Delirium in late life (not specifically surgery related) is associated with doubling the rate of cognitive decline<sup>37</sup> and greatly increases the risk of incident dementia.<sup>48</sup> It should therefore be a priority for surgery-related research to investigate if post-CABG delirium has similar impact on long-term cognitive decline and even dementia incidence.

Only 5 studies assessed cognitive decline in the long-term (>12 months post-CABG), restricting risk or protective factors that could be extracted. These analyses revealed no significant results, likely because of smaller sample sizes and study variability. Cognitive

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decline is seen in nearly 40% of patients 1 to 5 years post-CABG.<sup>4</sup> The presence of cognitive decline is associated with decreased quality of life, functional capacity, and increased rates of depression.<sup>7</sup> In addition, longer-term cognitive decline can lead to a loss of support networks, such as friends and neighbors, and can strain familial relationships.<sup>49</sup> Yet, from this meta-analysis, because of the lack of data at this time point, no possible risk reduction strategies can be suggested.

Meta-regressions generally found that age was not related to the pooled effect estimates. The 3 significant meta-regressions (delirium: ACC time and LOS in ICU; acute cognitive decline: CPB time) revealed a negative relationship with age, meaning as mean age of the study sample increased, the effect of the risk factor decreased. For example, as age increased, there was a smaller difference in ACC time between those who developed delirium and those who did not. These results could be influenced by older age increasing the risk of post-CABG complications (eq. AF, dialysis, reintubation, and stroke).<sup>50</sup> These complications are likely to increase LOS in the ICU, regardless of the presence of delirium or cognitive decline. In addition, because of increased complications, greater surgical precautions may be taken with older adults (eg, prioritizing dangerously stenosed arteries over complete revascularization of coronary arteries), which may decrease overall ACC and CPB time, minimizing group differences. Although these meta-regressions reached significance, most of the variance (≥50%) was not explained by age. Therefore, these risk factors should still be considered clinically meaningful.

This meta-analysis revealed multiple risk factors for post-CABG delirium and cognitive decline based on group-level data from included studies. Future research could identify clusters of risk factors by accessing patient-level data. This investigation could be guided by common risk factors identified in this meta-analysis, specifically depression, cognitive impairment, stroke history, diabetes mellitus, and vascular factors (hypertension and AF).

This is the only meta-analysis to investigate risk and protective factors for multiple outcomes (delirium and cognitive decline) across multiple time points in patients undergoing CABG. Although this study is not without limitations, the pooled sample size is >60 000 patients, allowing for greater generalizability of the results. The pooled results of this meta-analysis cannot be directly compared across time (for cognitive decline), as the same individuals are not represented at all time points. As only studies published in English were included, there may be a geographical bias. All extracted data within this meta-analysis were unadjusted for covariates, which does not permit investigation of independence. In addition, no temporal adjustments were conducted (eg, adjusting for preoperative depression

within the intraoperative and postoperative factor meta-analyses). Therefore, caution should be used in interpreting study results, especially on the utility of identified intraoperative and postoperative risk factors in risk prediction tools. Within the literature, substantially fewer articles investigated midterm and long-term cognitive decline (than acute cognitive decline), which means that there may be important risk factors for these time periods that our approach could not identify. Many analyses conducted herein resulted in medium to high heterogeneity. Investigation into small study effect (publication bias) generally did not change the conclusions of this study (Figures S2, S4, and S6). The heterogeneity may be partially driven by the wide range of tests, screening tools, and methods of classifying delirium and cognitive decline within the included studies (Tables S8 and S9), although, notably, our subgroup analyses for delirium diagnosis (when using a diagnostic tool versus no tool) revealed no meaningful differences (Table S7).

# CONCLUSIONS

There are many risk factors for delirium and cognitive decline (acutely and in the midterm) following CABG, which could be used in clinical practice, including the development or modification of a clinical prediction tool. Use of a CABG-specific risk tool could improve prognosis and, in turn, lead to better patient management. This is especially critical for delirium, as it is severely underrecognized and has serious outcomes.<sup>9</sup> To improve prediction ability of these risk tools, future development could also integrate the results of functional neuroimaging (eg, electroencephalography) and biomarker research, related to CABG.

The most clinically meaningful finding from this meta-analysis was the identification of modifiable preoperative risk factors for delirium and cognitive decline, of depression, diabetes mellitus, hypertension, and cognitive impairment. Improving the management of depression, diabetes mellitus, and hypertension in a preoperative setting may result in reductions in incident delirium and cognitive decline post-CABG. Targeting cognitive impairment through cognitive training interventions also has potential. Even if these are small reductions in incidence rates, they will have great impact at scale. Future work should investigate if we can target modifiable risk factors to reduce the incidence of delirium and cognitive decline post-CABG.

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#### Disclosures

None.

#### Supplementary Material

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# SUPPLEMENTAL MATERIAL

### Data S1.

### **Quality Assessment Tool**

# **Critical Appraisal Checklist for Cohort Studies & Studies Reporting Prevalence Data**

This checklist and scoring instructions, was developed for the purpose of our meta-analysis using checklists created by the Joanna Briggs Institute <sup>21, 22</sup>.

- 2 points: Sufficiently fulfilled
- 1 point: Partially fulfilled or unclear

0 points: Unfulfilled or not reported

	2	1	0
1. Were the study participants and the setting described in detail (i.e.,			
sample size, sex proportion, age, recruitment hospital)?			
2. Were valid and reliable methods used for the identification of the			
condition (i.e., cognitive decline or delirium)?*			
3. Was the condition measured in a standard, reliable way for all			
participants (i.e., were the assessors who administered the measures			
adequately trained)? If there was more than one assessor, were they similar			
in ability/experience?*			
4. Were appropriate procedures in place to minimise attrition?			
5. Was the follow-up time reported?			
6. Was follow up complete, and if not, were the reasons to loss to follow-			
up described (i.e., was there a clear and justifiable description of why			
participants dropped out or were excluded from the analysis)?			
•••			
Notes:			

\*For studies that reported data for more than one outcome (i.e., cognitive impairment and delirium) the point scheme was relative to all outcomes. That is, a study would only score 2 on these items if all outcomes/conditions were identified using valid and reliable tests (item 2), in a valid and reliable manner (item 3).

#### **Scoring Instructions**

# **1.** Were the study participants and the setting described in detail (i.e., sample size, sex proportion, age, recruitment hospital)?

The study sample should be described in sufficient detail so that other researchers can determine if it is comparable to the population of interest to them. That is, did the researchers provide details on sample size, sex proportion, age and hospital recruited from for either the total sample at baseline, or the sample of participants included in the analyses?

- 2 = All details reported
- 1 = Some details reported
- 0 = No details reported

# 2. Were valid and reliable methods used for the identification of the condition (i.e., cognitive impairment or delirium)?

Here we are looking for measurement or classification bias. Many health problems are not easily diagnosed or defined and some measures may not be capable of including or excluding appropriate levels or stages of the health problem. If the outcomes were assessed based on existing definitions or diagnostic criteria, then the answer to this question is likely to be yes. If the outcomes were assessed using observer reported, or self-reported scales, the risk of over- or under-reporting is increased, and objectivity is compromised. Importantly, determine if the measurement tools used were validated instruments as this has a significant impact on outcome assessment validity.

Studies that reported only delirium data were assigned 2 points for this item if they used a standardized cognition or delirium assessment, and 1 point if they used a recognized criteria or guidelines (e.g., the Society of Thoracic Surgeons (STS) definition or The Diagnostic and Statistical Manual of Mental Disorders criteria.

- 2 = All measures were standardized and validated
- 1 = Some measures were standardized and validated
- 0 = No measures were standardized and validated

# 3. Was the condition measured in a standard, reliable way for all participants (i.e., were the assessors who administered the measures adequately trained)? If there was more than one assessor, were they similar in ability/experience?

Were those involved in collecting data trained or educated in the use of the instrument/s? If there was more than one data collector, were they similar in terms of level of education, and clinical or research experience. Overall, was the condition measured in the same way for all participants?

- 2 = The paper states that the assessor or assessors were trained. If the assessors were stated to be psychologists, neuropsychologists or psychometrists it was assumed they were adequately trained.
- 1 = Researchers mention that the tests were administered by assessors/investigators but do not mention their experience or training
- 0 =No clear statement of who conducted the assessments

#### 4. Were appropriate procedures in place to minimize attrition?

Appropriate measures for minimizing attrition are systematic contact strategies (e.g., contacting participants three times; by letter, phone and email). A procedure would be considered inappropriate if it was not systematic (e.g., letting participants contact them, and therefore relying on their motivation).

If there was only one follow-up time that was <10 days and a strategy for minimizing attrition was not mentioned, the study was still assigned 2 points as the strategy was assumed not to be necessary (i.e., the patients were still in hospital). Also, studies that reported only delirium data were assigned 2 points using this same rationale, as the patients are assumed to still be in hospital during the delirium assessments.

- 2 = Studies that utilized a systematic contact strategy that was explicit and would be thought to lead to greater retention at follow-up, or N/A.
- 1 = Procedure mentioned (e.g., called participants) but not clear if the contact process was thorough
- 0 =No strategy mentioned

#### 5. Was the follow up time reported?

The time points for follow-up assessments should be clearly stated. Studies with multiple follow-up assessments were assigned 2 points for this item if all follow-up time points were clearly and precisely stated, 1 point if some of the time-points were clearly and precisely stated, or all time-points were stated, but inexactly (e.g., "6 weeks").

- 2 = When the participant were likely to be out of hospital at time of assessment, studies that reported a mean and SD of the number of days/months for all follow-ups were assigned 2 points. If the follow-up time was likely to be when the patient was in hospital (e.g., 3 days) it was assumed that this was a precise value and the study was awarded 2 points.
- 1 = Studies that report a vague/inexact follow-up time (e.g., 6 months), which is likely to have varied between participants, for some or all follow-ups
- 0 = Follow-up time not reported

#### 6. Was follow up complete, and if not, were the reasons to loss to follow up described?

Reporting of efforts to follow up participants that dropped out may be regarded as an indicator of a well conducted study. Therefore, this item is scored depending on whether a clear and justifiable description of why people were left out, excluded, dropped out, etc. was provided.

- 2 = Follow-up was complete, or if not, there was a statement of how many participants dropped out and for what reasons
- 1 = There is an unclear statement outlining reasons for drop-out and how many participants for each reason (i.e., reasons for drop-out are given but not how many participants for each reason)
- 0 = There was drop out but no mention of reasons why

# Table S1. Pooled estimates and corresponding effect size (OR, MD, SMD) for pre, intra,

and post-operative variables for delirium (1-7 days) post-CABG.

	Pooled Estimate				Heterog	geneity	Common
							effect size
Variable	<b>k</b> ( <b>n</b> )	OR/MD†/	95%CI	p value	$I^2$	Tau <sup>2</sup>	SMD
		SMD‡					
Pre-Operative (Categorical)							
Alcoholism	6 (994)	0.90	0.50—1.62	.721	13.45	0.08	0.06
Arrhythmia, incl. AF	15 (31746)	2.07	1.70—2.51	<.001	25.35	0.03	0.40
BMI >28 (including >30)	7 (16297)	1.16	0.74—1.80	.516	56.28	0.17	0.08
BMI $\geq$ 30 only	5 (1786)	1.57	1.05—2.37	.030	0	0	0.25
Cognitive impairment	7 (1039)	4.17	2.75—6.33	<.001	0	0	0.79
Depression	4 (580)	2.49	1.29—4.81	.006	29.16	0.13	0.50
Diabetes	30 (48465)	1.49	1.39—1.60	<.001	0	0	0.22
Dyslipidemia/Hyperlipidemia	13 (6449)	0.89	0.63—1.25	.502	51.79	0.18	0.06
Education>12years/high school	4 (567)	0.66	0.41—1.06	.088	0	0	0.23
Hypertension	27 (38362)	1.44	1.21—1.70	<.001	52.54	0.07	0.20
Sex (male)	35 (37851)	0.90	0.75—1.08	.263	53.35	0.10	0.06
Kidney injury	14 (25264)	1.94	1.50—2.52	<.001	27.49	0.05	0.37
Previous MI <30 days	5 (926)	1.54	0.90—2.65	.116	37.82	0.14	0.24
Previous MI history/ever	11 (10662)	1.17	0.98—1.39	.075	0	0	0.09
Previous stroke, TIA, CVA	15 (27127)	2.55	1.94—3.35	<.001	44.42	0.10	0.52
PVD	14 (16340)	1.98	1.48—2.64	<.001	38.76	0.09	0.38
Smoking current	14 (17825)	1.19	0.84—1.69	.321	72.37	0.24	0.10
Smoking current/history	21 (25813)	1.15	0.94—1.42	.174	56.81	0.09	0.08
Pre-Operative (Continuous)							
Age (years) *	28 (9303)	4.14†	2.95—5.34	<.001	78.61	7.14	0.49
	I			Į			ļ

BMI	5 (2143)	0.03†	-0.46-0.51	.915	0	0	0.01
Cognition: All tests	9 (887)	-0.58‡	-0.78— -0.37	<.001	34.11	0.03	0.58
Cognition: MMSE only	7 (621)	-1.14†	-1.91— -0.36	.004	77.72	0.68	0.52
Depression GDS	2 (233)	0.75†	-0.15—1.65	.101	0	0	0.30
Education (years)	6 (665)	-0.93†	-1.65—-0.20	.012	19.31	0.16	0.25
EuroSCORE *	10 (11199)	1.35†	0.58—2.12	.001	96.10	1.38	0.51
LVEF (%)	11 (3308)	1.25†	-0.69—3.19	.208	79.34	7.97	0.13
Intra-Operative (Continuous)							
ACC time (mins)	16 (7488)	5.97†	0.62—11.32	.029	90.65	101.19	0.29
CPB time (mins)	21 (12412)	7.41†	4.03—10.78	<.001	51.93	25.72	0.25
Duration of surgery (mins)	13 (3218)	20.53†	8.67—32.38	.001	75.96	325.89	0.35
Intubation time (hours)	11 (6693)	6.82†	2.44—11.20	.002	98.40	52.26	0.75
Number of grafts	8 (2731)	0.11†	-0.02—0.24	.084	34.30	0.01	0.13
Post-Operative (Categorical)							
Arrhythmia, incl. AF	16 (8809)	3.53	2.41—5.16	<.001	71.51	0.37	0.70
Post-Operative (Continuous)							
LOS in ICU (days)	14 (7177)	2.22†	1.32—3.13	<.001	97.84	2.69	1.20

Note: \* indicates potential small-study effect or publication bias, see (**Figure S2**) and for forest plots (**Figure S1**). Symbols following pooled estimates denote different effect sizes: indicating OR (no symbol), MD† and SMD‡. ACC= aortic cross-clamp, AF= atrial fibrillation, BMI= body mass index, CPB= cardiopulmonary bypass, CVA= cerebrovascular attack, GDS= geriatric depression scale, ICU= intensive care unit, k= number of estimates (number of studies), LOS= length of stay, LVEF= left ventricular ejection fraction, , MD= mean difference, MI= myocardial infarction, MMSE= mini mental state examination, n= pooled sample size, OR= odds ratio, PVD= peripheral vascular disease, SMD= standardized mean difference and TIA= transient ischemic attack..

Table S2. Pooled estimates and corresponding effect size (OR, MD, SMD) for pre, intra, and post-operative variables for acute cognitive decline (immediately up to 1-month) post-CABG.

		Pooled Estimate		Hetero	geneity	Effect size	
Variable	<b>k</b> ( <b>n</b> )	OR/MD†/	95%CI	p value	I <sup>2</sup>	Tau <sup>2</sup>	SMD
		SMD‡					
Pre-Operative (Categorical)							
Arrhythmia, incl. AF	7 (945)	1.24	0.76—2.04	.389	0	0	0.12
Cognitive impairment	4 (714)	1.11	0.71—1.73	.653	0	0	0.06
Depression	2 (330)	3.42	1.12—10.46	.031	61.53	0.40	0.68
Diabetes	17 (3008)	1.44	1.21—1.72	<.001	4.18	0.01	0.20
Dyslipidemia/Hyperlipidemia	6 (836)	1.16	0.74—1.84	.512	35.86	0.11	0.08
Hypertension	15 (2012)	1.91	1.45—2.53	<.001	34.10	0.09	0.36
Sex (male)	18 (2299)	1.03	0.82—1.29	.824	0	0	0.01
Kidney injury	4 (749)	1.21	0.40—3.72	.735	54.22	0.67	0.11
Previous MI <90 days	3 (418)	1.12	0.59—2.16	.724	0	0	0.07
Previous MI history/ever	7 (1011)	1.16	0.83—1.63	.394	25.17	0.05	0.08
Previous stroke, TIA, CVA	5 (745)	2.44	1.47—4.04	.001	0	0	0.49
PVD	4 (856)	1.09	0.42—2.83	.865	57.17	0.50	0.05
Smoking current/history	9 (1400)	1.03	0.64—1.66	.892	68.09	0.31	0.02
Pre-Operative (Continuous)							
Age (years) *	22 (2761)	2.69†	1.20-4.18	<.001	92.85	9.17	0.53
BMI	5 (906)	-0.20†	-0.25— -0.14	<.001	0	0	0.10
Cognition: All tests	3 (151)	0.23‡	-0.43—0.88	.492	69.56	0.23	0.23
Cognition: MMSE only	2 (116)	0.28†	-1.39—1.96	.740	82.66	1.21	0.24
Depression: All tests	4 (448)	0.50‡	-0.48—1.48	.316	93.32	0.92	0.50

Education (years)	6 (534)	-0.44†	-1.40—0.53	.377	49.52	0.65	0.11
EuroSCORE	4 (582)	0.74†	0.48—1.01	<.001	0	0	0.46
LVEF %	9 (1126)	-1.97†	-4.21—0.28	.086	72.49	8.28	0.21
Intra-Operative (Continuous)							
ACC time (mins)	7 (867)	-1.34†	-5.91—3.23	.566	61.81	20.52	0.07
CPB time (mins)	13 (1699)	3.39†	-0.10—6.88	.057	59.34	16.87	0.15
Duration of surgery (mins)	6 (723)	13.52†	3.67—23.38	.007	21.27	32.28	0.26
Intubation time (hours)	6 (1193)	1.95†	1.37—2.52	<.001	28.29	0.15	0.82
Number of grafts	7 (1113)	0.03†	-0.03—0.09	.400	7.50	0	0.10
Total microemboli	4 (771)	0.16‡	-0.070.38	.167	45.77	0.02	0.16
Post-Operative (Categorical)							
Arrhythmia, incl. AF	6 (1045)	1.40	1.01—1.94	.042	0	0	0.19
Delirium	3 (355)	6.15	2.32—16.27	<.001	6.32	0.07	1.00
Without outlier	2 (308)	4.85	1.89—12.45	.001	0	0	0.87
Post-Operative (Continuous)							
LOS in ICU (days)	7 (1055)	0.29†	0.04—0.55	.025	77.82	0.08	0.77

Note: \* indicates potential small-study effect or publication bias, see (**Figure S4**) and for forest plots (**Figure S3**). Symbols following pooled estimates denote different effect sizes: indicating OR (no symbol), MD† and SMD‡. ACC= aortic cross-clamp, AF= atrial fibrillation, BMI= body mass index, CPB= cardiopulmonary bypass, CVA= cerebrovascular attack, ICU= intensive care unit, k= number of estimates (number of studies), LOS= length of stay, LVEF= left ventricular ejection fraction, , MD= mean difference, MI= myocardial infarction, n= pooled sample size, OR= odds ratio, PVD= peripheral vascular disease, SMD= standardized mean difference and TIA= transient ischemic attack

Table S3. Pooled estimates and corresponding effect size (OR, MD, SMD) for pre, intra, and post-operative variables for cognitive decline in the mid-term (1 to 6-months) post-CABG.

	Pooled 1	Estimate		Hetero	geneity	Effect size
<b>k</b> ( <b>n</b> )	OR/MD†/	95%CI	p value	$\mathbf{I}^2$	Tau <sup>2</sup>	SMD
	SMD‡					
2 (471)	2.50	1.28—4.88	.007	0	0	0.51
10 (2046)	1.54	0.98—2.40	.059	61.33	0.28	0.24
12 (2599)	1.01	0.82—1.23	.965	0	0	0.00
12 (2350)	0.89	0.59—1.32	.558	69.32	0.31	0.07
3 (975)	0.88	0.57—1.37	.580	41.32	0.06	0.07
2 (761)	0.83	0.26—2.63	.748	0	0	0.11
2 (761)	0.71	0.41—1.21	.209	0	0	0.19
5 (1006)	1.00	0.73—1.37	.983	0	0	0.00
12 (2093)	1.09†	-0.06—2.25	.063	29.21	1.12	0.13
3 (855)	0.30‡	0.01—0.59	.041	68.84	0.04	0.30
2 (795)	0.50†	-0.17—1.17	.146	89.28	0.21	0.43
3 (429)	0.86‡	-0.68—2.39	.273	96.08	1.75	0.86
5 (950)	0.13†	-0.57—0.83	.715	44.26	0.24	0.05
7 (1266)	0.61†	-0.63—1.86	.336	0	0	0.06
4 (890)	-1.29†	-4.35—1.76	.407	0	0	0.06
7 (1266)	2.15†	-2.44—6.74	.359	28.63	10.41	0.06
4 (1124)	-0.06†	-0.17—0.06	.358	0	0	0.06
	2 (471) 10 (2046) 12 (2599) 12 (2350) 3 (975) 2 (761) 2 (761) 5 (1006) 12 (2093) 3 (855) 2 (795) 3 (429) 5 (950) 7 (1266) 4 (890) 7 (1266)	k (n)         OR/MD†/ SMD;           2 (471)         2.50           10 (2046)         1.54           12 (2599)         1.01           12 (2350)         0.89           3 (975)         0.88           2 (761)         0.83           2 (761)         0.71           5 (1006)         1.00           12 (2093)         1.09†           3 (855)         0.30‡           2 (795)         0.50†           3 (429)         0.86‡           5 (950)         0.13†           7 (1266)         0.61†           4 (890)         -1.29†           7 (1266)         2.15†	SMD;         2 (471)       2.50 $1.28-4.88$ 10 (2046) $1.54$ $0.98-2.40$ 12 (2599) $1.01$ $0.82-1.23$ 12 (2350) $0.89$ $0.59-1.32$ 3 (975) $0.88$ $0.57-1.37$ 2 (761) $0.83$ $0.26-2.63$ 2 (761) $0.71$ $0.41-1.21$ 5 (1006) $1.00$ $0.73-1.37$ 12 (2093) $1.09^{\dagger}$ $-0.06-2.25$ 3 (855) $0.30^{\ddagger}$ $0.01-0.59$ 2 (795) $0.50^{\dagger}$ $-0.17-1.17$ 3 (429) $0.86^{\ddagger}_{\pm}$ $-0.68-2.39$ 5 (950) $0.13^{\dagger}_{\mp}$ $-0.63-1.86$ 4 (890) $-1.29^{\dagger}_{\mp}$ $-4.35-1.76$ 7 (1266) $2.15^{\dagger}_{\mp}$ $-2.44-6.74$	k (n)OR/MD†/95%CIp value $2 (471)$ $2.50$ $1.28-4.88$ .007 $10 (2046)$ $1.54$ $0.98-2.40$ .059 $12 (2599)$ $1.01$ $0.82-1.23$ .965 $12 (2350)$ $0.89$ $0.59-1.32$ .558 $3 (975)$ $0.88$ $0.57-1.37$ .580 $2 (761)$ $0.83$ $0.26-2.63$ .748 $2 (761)$ $0.71$ $0.41-1.21$ .209 $5 (1006)$ $1.00$ $0.73-1.37$ .983 $12 (2093)$ $1.09^{\dagger}$ $-0.06-2.25$ .063 $3 (855)$ $0.30^{\ddagger}_{+}$ $0.01-0.59$ .041 $2 (795)$ $0.50^{\dagger}_{+}$ $-0.17-1.17$ .146 $3 (429)$ $0.86^{\ddagger}_{+}$ $-0.68-2.39$ .273 $5 (950)$ $0.13^{\dagger}_{+}$ $-0.57-0.83$ .715 $7 (1266)$ $0.61^{\dagger}_{+}$ $-0.63-1.86$ .336 $4 (890)$ $-1.29^{\dagger}_{+}$ $-4.35-1.76$ .407 $7 (1266)$ $2.15^{\dagger}_{+}$ $-2.44-6.74$ .359	k (n)OR/MD†/95%CIp value $I^2$ 2 (471)2.501.28—4.88.007010 (2046)1.540.98—2.40.05961.3312 (2599)1.010.82—1.23.965012 (2350)0.890.59—1.32.55869.323 (975)0.880.57—1.37.58041.322 (761)0.830.26—2.63.74802 (761)0.710.41—1.21.20905 (1006)1.000.73—1.37.983012 (2093)1.09†-0.06—2.25.06329.213 (855)0.30‡0.01—0.59.04168.842 (795)0.50†-0.17—1.17.14689.283 (429)0.86‡-0.68—2.39.27396.085 (950)0.13†-0.57—0.83.71544.267 (1266)0.61†-0.63—1.86.33604 (890)-1.29†-4.35—1.76.40707 (1266)2.15†-2.44—6.74.35928.63	k (n)       OR/MD†/       95%CI       p value       I²       Tau²         2 (471)       2.50 $1.28-4.88$ .007       0       0         10 (2046) $1.54$ $0.98-2.40$ .059 $61.33$ $0.28$ 12 (2599) $1.01$ $0.82-1.23$ .965       0       0         12 (2350) $0.89$ $0.59-1.32$ .558       69.32 $0.31$ 3 (975) $0.88$ $0.57-1.37$ .580       41.32 $0.06$ 2 (761) $0.71$ $0.41-1.21$ .209       0       0         5 (1006) $1.00$ $0.73-1.37$ .983       0       0         12 (2093) $1.09^{\dagger}$ $-0.06-2.25$ .063       29.21 $1.12$ 3 (855) $0.30^{\ddagger}$ $0.01-0.59$ .041       68.84       0.04         2 (795) $0.50^{\dagger}$ $-0.17-1.17$ .146       89.28       0.21         3 (429) $0.86^{\ddagger}_{\pm}$ $-0.68-2.39$ .273       96.08       1.75         5 (950) $0.13^{\dagger}_{\pm}$ $-0.57-0.83$ .715       44.26       0.24         7 (1266)

Total microemboli	4 (542)	-0.46‡	-0.97—0.05	.076	51.03	0.12	0.46
Post-Operative (Continuous)							
LOS in ICU (days)	2 (100)	0.23†	-1.10—1.55	.736	88.27	0.80	0.33

Note: \* indicates potential small-study effect or publication bias, see (**Figure S6**) and for forest plots (**Figure S5**). Symbols following pooled estimates denote different effect sizes: indicating OR (no symbol), MD† and SMD‡. ACC= aortic cross-clamp, CI= cognitive index score, CPB= cardiopulmonary bypass, CVA= cerebrovascular attack, ICU= intensive care unit, k= number of estimates (number of studies), LOS= length of stay, LVEF= left ventricular ejection fraction, , MD= mean difference, MI= myocardial infarction, n= pooled sample size, OR= odds ratio, PVD= peripheral vascular disease, SMD= standardized mean difference and TIA= transient ischemic attack. Table S4. Pooled estimates and corresponding effect size (OR, MD, SMD) for pre, intra, and post-operative variables for cognitive decline in the long-term (12 to 15-months) post-CABG.

		Poole	ed Estimate		Hetero	geneity	Effect size
Variable	k (n)	OR/MD†/	95%CI	p value	I <sup>2</sup>	Tau <sup>2</sup>	SMD
		SMD‡					
Pre-Operative (Categorical)							
Cognitive impairment	2 (343)	1.02	0.57—1.80	.952	0	0	0.01
Diabetes	2 (504)	1.44	0.78—2.64	.245	0	0	0.20
Sex (male)	2 (301)	1.17	0.28—4.91	.830	28.63	0.49	0.09
Hypertension	2 (504)	1.30	0.84—2.00	.241	0	0	0.14
Pre-Operative (Continuous)							
Age (years)	2 (301)	1.57†	-2.94—6.09	.495	46.03	5.30	0.17
7 Intra-Operative (Continuous)							
Number of grafts	2 (301)	0.03†	-0.27—0.33	.832	0	0	0.04

Note: \* indicates potential small-study effect or publication bias. See (**Figure S7**) for forest

plots. Symbols following pooled estimates denote different effect sizes: indicating OR (no symbol), MD<sup>†</sup> and SMD<sup>‡</sup>. k= number of estimates (number of studies), MD= mean difference, n= pooled sample size, OR= odds ratio, SMD= standardized mean difference.

# Table S5. Excluded references from full-text screening with associated reason.

Reference	Exclusion Reason
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Anonymous. Alzheimer's gene linked with postoperative confusion. Journal of psychosocial nursing and mental health services. 1998;36:13-14	abstract only
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Anaesthesia. 2013;68:571-575	operationalised
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Ovchinnikov DA, Amosov DD, Vorobyov EA, Garnyuk VV, Beltiukov PP, Grebennik VK, Gordeev ML, Barantsevich ER. [cognitive dysfunction and content of inflammatory markers in patients after coronary artery bypass graft]. Zhurnal Nevrologii i Psikhiatrii Imeni S.S. Korsakova. 2017;117:5-10	not in english
Ozturk T, Kocan AA, Yildirim F, Alp D, Kurdal T. The effect of beta-blocking agents on morbidity und mortality following coronary artery bypass surgery. Gogus-Kalp-Damar Anestezi ve Yogun Bakim Dernegi Dergisi. 2013;19:80-85	not in english
Petrova MM, Prokopenko SV, Eremina OV, Matjushin GV, Sakovich VA, Drobot DB, Mozhejko EY, Kaskaeva DS. No title. Rational Pharmacotherapy in Cardiology. 2015;11:391-397	not in english
Petrova MM, Prokopenko SV, Eremina OV, Mozheiko EY, Kaskaeva DS, Gankin MI. Cerebral circulation and cognitive status of coronary heart disease patients after bypass surgery. [russian]. Russian Journal of Cardiology. 2017;149:34-41	not in english
Petrova MM, Prokopenko SV, Eremina OV, Mozhejko EY, Kaskaeva DS. Correction of postoperative cognitive dysfunction in cardiosurgery using computer- based stimulation programs. Zhurnal Nevrologii i Psihiatrii imeni S.S. Korsakova. 2016;116:35-41	not in english
Petrova MM, Prokopenko SV, Eremina OV, Mozheyko EY, Kaskaeva DS, Gankin MI. Cerebral circulation and cognition in patients with coronary heart disease underwent coronary bypass operation. [russian]. Russian Journal of Cardiology. 2017;143:77-84	not in english
Petrova MM, Shprakh VV, Kaskaeva DS, Eremina OV, Narkevich AN, Eremina SS. Prognostic methods of postoperative cognitive dysfunction in patients with ischemic heart disease after coronary bypass surgery under extracorporeal circulation. [russian]. Zhurnal nevrologii i psikhiatrii imeni S.S. 2018;Korsakova. 118:81-86	not in english
Pfeiffer T, Siepe M, Benk C, Gieringer A, Zemann S, Schlensak C, Beyersdorf F. Influence of a changed perfusion management with increased perfusion pressure in heart-lung machine on the postoperative neuropsychological capabilities of the patient. Kardiotechnik. 2011;20:3-7	not in english
Polushin AY, Yanishevskiy SN, Maslevtsov DV, Krivov VO, Beskrovnaya OV, Molchan NS. The efficacy of prevention of postoperative cognitive dysfunction in cardiac surgeries with the use of the cerebrolysin. [russian]. Zhurnal Nevrologii i Psihiatrii imeni S.S. 2017;Korsakova. 117:37-45	not in english

Rodig G, Taeger K. 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	not in english
Rothenhausler HB, Stepan A, Hetterle R, Trantina-Yates A. The effects of coronary artery bypass graft surgery on health-related quality of life, cognitive performance, and emotional status outcomes: A prospective 6-month follow-up consultation-liaison psychiatry study. Fortschritte der Neurologie Psychiatrie.	not in english
2010;78:343-354 Sezer O, Karlidag R, Karabulut AB, Ozcan C, Nisanoglu V, Turkoz Y, But A, Unal S. Relationship between nitric oxide levels and delirium in patients with coronary bypass operation. Klinik Psikofarmakoloji Bulteni. 2004;14:185-190	not in english
Solodukhin AV, Bezzubova VA, Kuhareva IN, Inozemtseva AA, Seryy AV, Yanitskiy MS, Trubnikova OA, Barbarash OL. The relationship between psychological characteristics of the attitude to the disease, coping behavior of patients with ischemic heart disease, and their cognitive status. RUDN Journal of Psychology and Pedagogics. 2017;14:178-189	not in english
Stevens R, Gersbach P, Ruchat P, Hurni M, Stumpe F, Fischer A, Sadeghi H. [cardiac surgery in octogenarians]. Chirurgie cardiaque chez l'octogenaire. 1995;125:2084-2089	not in english
Sugimoto K, Ohata A, Terada H, Kuriyama Y. Changes in neuropsychological functions following cardiovascular surgery. Clinical Neurology. 1995;35:606-610	not in english
Thiel A, Zimmer M, Stertmann WA, Kaps M, Hempelmann G. Microembolisations during cardiac surgery under extracorporeal circulation. Anasthesiologie Intensivmedizin Notfallmedizin Schmerztherapie. 1997;32:715-720	not in english
Trubnikova O, Mamontova A, Maleva O, Kuhareva I, Barbarash O. Factors determining the development of long-term postoperative cognitive dysfunction in patients with type 2 diabetes undergoing coronary artery bypass grafting. European Journal of Preventive Cardiology. 2015;22:S189	not in english
Trubnikova OA, Maleva OV, Tarasova IV, Mamontova AS, Uchasova EG, Barbarash OL. Effect of statins on development of early cognitive dysfunction after coronary artery bypass grafting. Kardiologiia. 2015;55:49-56	not in english
Trubnikova OA, Mamontova AS, Maleva OV, Tarasova IV, Kukhareva IN, Kuzmina AA, Kagan ES, Barbarash OL. Predictors of persistant post-operation cognitive dysfunction in 2 type diabetes patients after coronary bypass grafting. Russian Journal of Cardiology. 2016;130:12-18	not in english
Trubnikova OA, Mamontova AS, Syrova ID, Kukhareva IN, Maleva OV, Barbarash OL. The cognitive status of patients with type 2 diabetes mellitus after coronary bypass surgery. Klinicheskaia Meditsina. 2015;93:39-44	not in english
Trubnikova OA, Mamontova AS, Tarasova IV, Maleva OV, Kuz'mina AA, Barbarash OL. Association of cognitive impairments with carbohydrate and lipid metabolic parameters in type 2 diabetes mellitus patients undergoing coronary bypass surgery. Terapevticheskii Arkhiv. 2015;87:69-75	not in english
Trubnikova OA, Tarasova IV, Mamontova AS, Syrova ID, Maleva OV, Barbarash OL. A role of carotid stenoses in the structure of early postoperative cognitive dysfunction in patients underwent coronary artery bypass grafting. Zhurnal Nevrologii i Psikhiatrii Imeni S.S. Korsakova. 2014;114:36-42	not in english
Trubnikova OA, Tarasova IV, Mamontova AS, Syrova ID, Maleva OV, Barbarash OL. Structure of cognitive disorders and dynamics of bioelectric activity of the brain in patients after direct myocardial revascularization. Russian Journal of Cardiology. 2014;112:57-62	not in english
Trubnikova OA, Tarasova IV, Syrova ID, Mamontova AS, Kovalenko AV, Barbarash OL, Barbarash LS. Neuropsychological status of patients with low and moderate carotid artery stenoses after the coronary artery bypass surgery. Zhurnal Nevrologii i Psihiatrii imeni S.S. Korsakova. 2013;113:28-33	not in english
Tsygan NV, Odinak MM, Khubulava GG, Tsygan VN, Peleshok AS, Andreev RV, Kurasov ES, Litvinenko IV. [postoperative cerebral dysfunction]. Zhurnal Nevrologii i Psikhiatrii Imeni S.S. Korsakova. 2017;117:34-39	not in english
Valentini M, Spezzaferri R, Brambilla G, Tavanelli M, Sangiuliano M, Majorino G, Racca V, Ferratini M. Complexities of psychological disorders observable after surgical myocardial revascularization in male subjects. Italian Heart Journal Supplement. 2005;6:375-381	not in english
Wos S, Opala G, Jasinski M, Janas P, Bachowski R, Kus H, Domaradzki W, Gemel M, Deja M, Dyaczynska-Herman A. The incidence of early central nervous	not in english

Xu BL, Bi Q, Chen MY, Luo D. Ct cerebral perfusion parameters in prediction of postoperative cognition disorders of off-pump coronary artery bypass grafting. Chinese Journal of Interventional Imaging and Therapy. 2015;12:298-302	not in english
Xu D, Liu F, Hua Y, Zhang K-f, Liu Y-h, Shang X-b, Li H-l, Yao Q, Li X-f, Zhang R, et al. Increasing cardiopulmonary bypass flow volume improves outcome of patient with carotid stenosis undergoing coronary artery bypass grafting. Zhonghua wai ke za zhi [Chinese journal of surgery]. 2009;47:577-579	not in english
Yilmaz E, Aksun M, Girgin S, Gulseren S, Kuru V, Sencan A, Koroglu L, Aran G, Karahan N. The comparison of the effects of the off-pump and cardiopulmonary by-pass techniques upon postoperative delirium at elective coronary by-pass greft surgery. Gogus-Kalp-Damar Anestezi ve Yogun Bakim Dernegi Dergisi. 2013;19:67-75	not in english
Yilmaz M, Aydin U, Kilic Yilmaz V, Yavuz Y, Denizalti TB, Canik S. The effect of magnesium on neurocognitive functions after cardiopulmonary by-pass surgery. Turkiye Klinikleri Cardiovascular Sciences. 2014;26:105-110	not in english
Yin Y-q, Luo A-l, Guo X-y, Li L-h, Ren H-z, Ye T-h, Huang Y-g. Perioperative cortisol circadian secretion and neuropsychological states in patients undergoing coronary artery bypass grafting surgery. Zhonghua wai ke za zhi [Chinese journal of surgery]. 2005;43:463-467	not in english
Zhang Y, Cheng H, Xu C, Bao H, Shi H, Ge Y, Wei H. [effects of ultrasound-guided stellate ganglion block on cerebral oxygen metabolism and postoperative cognitive dysfunction in the elderly]. Sheng wu yi xue gong cheng xue za zhi = Journal of biomedical engineering = Shengwu yixue gongchengxue zazhi. 2014;31:1107-1110	not in english
Zhang Y, Qian Y, Bao H, Shi H, Zhou J. Effect of stellate ganglion block on bilateral regional cerebral oxygen saturation and postoperative cognitive function. Sheng wu yi xue gong cheng xue za zhi = Journal of biomedical engineering = Shengwu yixue gongchengxue zazhi. 2016;33:132-135	not in english
Zhao YH, Wen DX. Analysis of related factors of postoperative cognitive dysfunction for patients undergoing off-pump coronary artery bypass graft surgery. Journal of Shanghai Jiaotong University (Medical Science). 2016;36:100-104	not in english
Zoll A, Degirmenci U, Bleich S, Richter-Schmidinger T, Kornhuber J, Fischlein T, Weih M. Neuropsychological complications after coronary bypass grafting. Fortschritte der Neurologie-Psychiatrie. 2009;77:97-101	not in english
Ernest CS, Elliott PC, Murphy BM, Le Grande MR, Goble AJ, Higgins RO, Worcester MUC, Tatoulis J. Predictors of cognitive function in candidates for coronary artery bypass graft surgery. Journal of the International Neuropsychological Society : JINS. 2007;13:257-266	only baseline data
Ernest CS, Murphy BM, Worcester MUC, Higgins RO, Elliott PC, Goble AJ, Le Grande MR, Genardini N, Tatoulis J. Cognitive function in candidates for coronary artery bypass graft surgery. The Annals of thoracic surgery. 2006;82:812-818	only baseline data
Hudetz JA, Patterson KM, Pagel PS. 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;29:320-325	only baseline data
Tsushima WT, Johnson DB, Lee JD, Matsukawa JM, Fast KMS. Depression, anxiety and neuropsychological test scores of candidates for coronary artery bypass graft surgery. Archives of clinical neuropsychology : the official journal of the National Academy of Neuropsychologists. 2005;20:667-673	only baseline data
Aldea GS, O'Gara P, Shapira OM, Treanor P, Osman A, Patalis E, Arkin C, Diamond R, Babikian V, Lazar HL, et al. Effect of anticoagulation protocol on outcome in patients undergoing cabg with heparin-bonded cardiopulmonary bypass circuits. The Annals of thoracic surgery. 1998;65:425-433	other
Barry SJE, Zeger SL, Selnes OA, Grega MA, Borowicz LM, Jr., McKhann GM. Quantitative methods for tracking cognitive change 3 years after coronary artery bypass surgery. The Annals of thoracic surgery. 2005;79:1104-1109	other
Bhamidipati D, Goldhammer JE, Sperling MR, Torjman MC, McCarey MM, Whellan DJ. Cognitive outcomes after coronary artery bypass grafting. Journal of Cardiothoracic & Vascular Anesthesia. 2017;31:707-718	other
Cockburn J, Hildick-Smith D, Trivedi U, De Belder A. Coronary revascularisation in the elderly. Heart. 2017;103:316-324	other
Indja B, Fanning JP, Maller JJ, Fraser JF, Bannon PG, Vallely M, Grieve SM. Neural network imaging to characterize brain injury in cardiac procedures: The emerging utility of connectomics. British Journal of Anaesthesia. 2017;118:680-688	other

Lamy A, Devereaux PJ, Prabhakaran D, Hu S, Piegas LS, Straka Z, Paolasso E, Taggart D, Lanas F, Akar AR, 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. American Heart Journal. 2012;163:1-6	other
Wu M, Liang Y, Dai Z, Wang S. Perioperative dexmedetomidine reduces delirium after cardiac surgery: A meta-analysis of randomized controlled trials. Journal of Clinical Anesthesia. 2018;50:33-42	other
Yuan SM, Lin H. Postoperative cognitive dysfunction after coronary artery bypass grafting. Brazilian Journal of Cardiovascular Surgery. 2019;34:76-84	other
Maggio M, Nicolini F, Cattabiani C, Beghi C, Gherli T, Schwartz RS, Valenti G, Ceda GP. Effects of testosterone supplementation on clinical and rehabilitative outcomes in older men undergoing on-pump cabg. Contemporary Clinical Trials. 2012;33:730-738	protocol paper
Uva MS, Matias F, Cavaco S, Magalhaes MP. 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;9:44	protocol paper
Whitlock R, Teoh K, Vincent J, Devereaux PJ, Lamy A, Paparella D, Zuo Y, Sessler DI, Shah P, Villar JC, et al. Rationale and design of the steroids in cardiac surgery trial. American Heart Journal. 2014;167:660-665	protocol paper

 Table S6. Demographic data, presence in statistical analyses and quality assessment scores for included studies within risk and

 protective factor meta-analyses for delirium and cognitive-decline post CABG.

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
Kel. INO.	Leau Author, Tear	Patients	of Males	Age	of Age	CI	C2	ĊĴ	Dei	(/12)
51	Al Tmimi, 2016	92	78	67	R: 46-86	-	-	-	Х	12
52	Baba, 2007	218	152	71.25	5.5	Х	-	-	-	10
53	Boodhwani, 2006*	448	390	68.3	0.4	X	-	-	-	12
54	Braekken, 1998	14	14	N/A	N/A	-	X	-	-	7
55	Bucerius, 2005	9682	7500	N/A	N/A	-	-	-	X	6
56	Caldas 2019	67	51	64.3	9.5	-	-	-	X	12
57	Chen, 2017	136	104	60.85	7.76	-	-	-	X	10
58	Christiansen, 2016	8	7	63.38	10.69	X	-	-	-	7
59	Coffey, 1983	1669	1384	52.15	SEM: 8	-	-	-	X	7
60	Colak, 2015	190	148	62.66	7.96	X	-	-	-	7
61	Cumurcu, 2008	50	37	59.62	10.66	-	-	-	X	9

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
		Patients	of Males	Age	of Age	UI	0	00	Der	(/12)
62	deTournay-Jette, 2011	61	51	70.39	4.69	Х	Х	-	-	10
63	Dieleman, 2009	281	192	61.3	9	-	Х	Х	-	10
64	Djaiani, 2003	417	293	60.34	10	-	Х	-	-	9
65	Dong, 2014	108	83	63	7.9	Х	-	-	Х	10
66	Eriksson, 2002	52	40	70.27	5.53	-	-	-	Х	12
67	Goto, 2000	177	117	70.26	4.99	X	-	-	-	11
68	Gottesman, 2010	5052	3682	63.92	N/A	-	-	-	X	7
69	Hall, 1999	35	27	65.9	9.1	X	-	-	-	12
70	Harmon, 2004 <sup>†</sup>	35	28	61.7	7.51	X	Х	-	-	9
71	Harmon, 2005 <sup>†</sup>	36	30	64.07	N/A	X	-	-	-	12
72	Humphreys, 2016	173	148	63.47	10.1	-	-	-	X	7
73	Kadoi, 2001 <sup>‡</sup>	185	138	N/A	N/A	X	X	-	-	6
74	Kadoi, 2002§	60	53	62.75	8.5	-	Х	-	-	9

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
<b>Kei</b> . 100.	Leau Author, Tear	Patients	of Males	Age	of Age	CI	02	CJ	Dei	(/12)
75	Kadoi, 2003 <sup>‡</sup>	180	136	65	9	-	X	-	-	9
76	Kadoi, 2005§	280	210	65.07	9.93	X	X	-	-	9
77	Kadoi, 2007§	106	53	62.55	10.45	-	X	-	-	9
78	Kadoi, 2011 (a)§	124	89	61.29	5.39	X	-	-	-	12
79	Kadoi, 2011 (b)§	90	68	65	9	X	X	-	-	9
80	Kazmierski, 2014 (a) <sup> ¶</sup>	113	90	64	R: 59-71	-	-	-	X	12
81	Kazmierski, 2014 (b) <sup>¶</sup>	102	N/A	N/A	N/A	-	-	-	X	12
82	Kazmierski, 2014 (c) <sup> ¶</sup>	113	90	Med: 64	R: 59-71	-	-	-	X	12
83	Khan, 2014	735	577	55.64	9.65	-	-	-	X	10
84	Khatri, 1999	170	127	61	10	-	X	-	-	7
85	Kok, 2017	57	N/A	N/A	N/A	-	-	X	-	5
86	Kumpaitiene, 2019	59	34	66.49	8.04	X	-	-	-	11
87	Lachmann, 2018	252	180	61.0	9.1	-	-	X	-	8

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
		Patients	of Males	Age	of Age					(/12)
88	Leenders, 2018	357	304	66.20	8.84	-	-	-	Х	9
89	Li, 2015	38	34	62.4	11.8	-	-	-	Х	10
90	Liu, 2009	227	209	60	8	Х	Х	-	-	9
91	Loponen, 2008	300	237	66.17	8.89	-	-	-	Х	8
92	Mardani, 2012	196	183	61.84	11.83	-	-	-	Х	9
93	Mariscalco, 2012	4079	3220	67.8	9.2	-	-	-	Х	12
94	Martin, 2010 <sup>#</sup>	14262	10912	N/A	N/A	-	-	-	Х	5
95	Martin, 2012 <sup>#</sup>	8474	6391	N/A	N/A	-	-	-	Х	7
96	Mathew, 2006**	121	N/A	N/A	N/A	-	Х	-	-	8
97	Mathew, 2007**	677	471	61.7	10.5	-	Х	-	-	9
98	Miyazaki, 2011	768	N/A	N/A	N/A	-	-	-	Х	6
99	Mu, 2010	243	200	61	8.3	-	-	-	Х	12
100	Mu, 2013	166	141	60	8.9	Х	-	-	-	12

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
Kel. 100.	Leau Autior, Tear	Patients	of Males	Age	of Age	CI	02	CJ	Dei	(/12)
101	Newman, 1987	67	62	55.0	7.8	X	-	-	-	10
102	Nikolic, 2012	370	271	N/A	N/A	-	-	-	X	7
103	Norkiene, 2007	1367	1035	64.98	9.14	-	-	-	X	10
104	Norkiene, 2011	127	103	60.91	7.24	X	-	-	-	11
105	Oh, 2008	46	36	63	5.5	X	-	-	-	11
106	Oh, 2017	292	211	N/A	N/A	-	-	-	X	10
107	Oldham, 2015	102	76	65.1	9	-	-	-	X	11
108	Oldham, 2019	131	96	65.8	9.2	-	-	-	X	12
109	Omiya, 2015	88	N/A	69	7	-	-	-	X	10
110	Otomo, 2013	153	109	72	7	-	-	-	X	12
111	Palmbergen, 2012	642	452	68.5	9.79	-	-	-	X	11
112	Plaschke, 2010	114	89	68.98	8.39	-	-	-	X	12
113	Reents, 2002	47	41	60.4	8	Х	_	-	_	10

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
	Lead Humbr, Tear	Patients	of Males	Age	of Age	Ċ1	02	00	Du	(/12)
114	Restrepo, 2002	13	10	65	9	X	-	-	-	10
115	Ringaitiene, 2015	99	70	67.6	7.78	-	-	-	Х	10
116	Robson, 2000	124	N/A	59.44	9.25	-	Х	-	-	7
117	Rodriguez, 2010	356	325	63	9	Х	Х	-	-	5
118	Rolfson, 1999 (a) <sup>††</sup>	75	59	N/A	N/A	-	-	-	X	12
119	Rolfson, 1999 (b) <sup>††</sup>	71	57	71	N/A	-	-	-	X	11
120	Royse, 2000	47	37	64.22	1.78	X	X	-	-	8
121	Royse, 2011	180	153	62.79	10.5	-	-	-	X	10
122	Rudolph, 2005	36	36	68.8	9.2	-	-	-	X	12
123	Rudolph, 2006 <sup>‡‡</sup>	80	62	74.9	6.2	-	-	-	X	11
124	Rudolph, 2009 <sup>‡‡</sup>	68	67	70.7	8.2	-	-	-	X	12
125	Sahan, 2018	40	34	65.85	6.02	X	X	-	-	9
6	Santos, 2004	220	142	70.71	5.48	-	-	-	Х	11

Ref. No.	Lood Author Voor	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
Kel. No.	Lead Author, Year	Patients	of Males	Age	of Age	CI	C2	C3	Dei	(/12)
126	Scott, 2002	103	84	64.77	1.3	Х	-	-	-	12
127	Sevuk, 2015	200	128	70.65	3.95	-	-	-	Х	12
128	Siepe, 2011	92	74	66.87	8.98	-	-	-	Х	12
129	Silbert, 2006 <sup>§§</sup>	326	252	67.9	7.6	X	X	-	-	9
130	Silbert, 2008 <sup>§§</sup>	264	203	67.8	7.7	X	-	X	-	7
131	Slater, 2009	240	201	64.74	9.96	X	X	-	-	7
132	Smith, 1986	55	51	54.7	R: 37-74	Х	-	-	-	9
133	Smith, 2000	381	308	N/A	N/A	-	Х	-	-	8
134	Stump, 1996	167	138	61	10	Х	-	-	-	8
135	Subramaniam, 2019	120	101	Med: 69	IQR: 63-76	-	-	-	X	12
136	Suksompong, 2002	110	110	61.95	7.58	X	-	-	-	10
137	Swaminathan, 2002	282	201	61	10.44	-	X	-	-	8
138	Sylivris, 1998	41	31	69.8	6.9	X	-	-	-	10

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	C3	Del	QA
<b>Kei</b> . 190.	Leau Aution, Tean	Patients	of Males	Age	of Age	CI	02	CJ	Dei	(/12)
139	Tagarakis, 2007	137	99	69.55	7.63	-	-	-	X	7
140	Tamura, 2019	88	76	69.3	2.5	-	-	-	X	10
141	Toeg, 2013 <sup>*</sup>	652	576	64.37	9	X	-	-	-	10
142	Trubnikova, 2014	101	101	56.6	5.85	X	-	X	-	4
143	Tully, 2010	158	125	64.68	10.56	-	-	-	X	10
144	van Dijk, 2004	281	191	61.2	9.0	-	X	-	-	7
145	Yilmaz, 2016	137	105	61.02	7.83	-	-	-	X	10
146	Zhang, 2015	249	197	62.9	9.34	-	-	-	X	12

<sup>†, ‡, §, ¶, ‡‡</sup> Suspected overlap of samples; <sup>\*, |, #, \*\*, ††, §§</sup> Known overlap of sample

Ref No. = supplementary reference list number; C1= acute cognitive decline (immediately post-operatively up to 1-month); C2= mid-term cognitive decline (1 to 6-months post-operatively); C3= long-term cognitive decline (12 to 15-months post-operatively). Del = delirium; Med = median; IQR= inter quartile range; QA = quality assessment; SD = standard deviation.

## Table S7. Subgroup meta-analyses of diagnostic tool, for pre, intra and post-operative

## variables for the development of delirium following CABG.

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Variable	ble Delirium Pooled Estimate Diagnosis k (n) OR/MD*/ 95%CI p valu						ogeneity Tau²
			<b>SMD</b> †				
Pre-Operative (Categorical)							
Alcoholism	No Tool		Insufficien	t Data			
	Tool	5 (694)	0.77	0.46—1.29	.317	0	0
Arrhythmia, incl. AF	No Tool	7 (31550)	2.05	1.77—2.37	<.001	0	0
	Tool	8 (1252)	1.91	1.15—3.16	<.001	45.09	0.21
BMI >28 (including >30)	No Tool	2 (15629)	0.86	0.51—1.47	.587	62.68	0.10
	Tool	5 (668)	1.46	0.89—2.41	.133	11.02	0.04
BMI $\geq$ 30 only	No Tool		Insufficien	t Data			
	Tool	4 (419)	1.85	1.09—3.14	.023	0.00	0
Cognitive Impairment	No Tool		Insufficien	t Data			
	Tool	6 (790)	4.11	2.59—6.53	<.001	0	0
Depression	No Tool	2 (378)	2.06	0.75—5.67	.162	66.06	0.35
	Tool	2 (202)	4.14	1.37—12.51	.012	0	0
Diabetes	No Tool	12 (42736)	1.46	1.33—1.60	<.001	13.34	0
	Tool	18 (5419)	1.57	1.32—1.87	<.001	0	0
Dyslipidaemia/Hyperlipidaemia	No Tool	4 (2283)	0.70	.033—1.49	.355	66.26	0.39
	Tool	9 (4166)	0.99	0.67—1.45	.943	46.78	0.14
Education>12years/high school	No Tool		Insufficien	t Data			
	Tool	3 (347)	0.78	0.45—1.35	.374	0	0
Hypertension	No Tool	11 (33054)	1.65	1.38—1.98	<.001	50.98	0.04
	Tool	16 (5308)	1.18	0.88—1.57	.267	38.51	0.12
Sex (male)	No Tool	10 (30814)	1.10	0.87—1.40	.415	62.44	0.06
	Tool	25 (6639)	0.78	0.60—1.01	.056	41.95	0.16
Kidney injury	No Tool	6 (23602)	1.91	1.40—2.60	<.001	36.40	0.05

Variable	Delirium Diagnosis	k (n)	Pooled E OR/MD*/	stimate 95%CI	p value	Hetero I <sup>2</sup>	ogeneity Tau <sup>2</sup>
			<b>SMD</b> †				
	Tool	8 (1662)	1.96	1.18—3.25	.009	29.13	0.14
Previous MI <30 days	No Tool	3 (101)	1.98	0.88—4.49	.100	52.09	0.27
	Tool	2 (200)	1.04	0.56—1.93	.909	0	0
Previous MI history/ever	No Tool	3 (6877)	1.04	0.72—1.51	.822	45.06	0.05
	Tool	8 (3785)	1.24	0.92—1.67	.160	0	0
Previous stroke, TIA, CVA	No Tool	6 (22297)	2.73	1.92—3.88	<.001	56.18	0.09
	Tool	9 (4830)	2.37	1.50—3.70	<.001	35.96	0.16
PVD	No Tool	4 (11604)	2.11	1.73—2.58	<.001	0.90	0
	Tool	10 (4736)	2.01	1.28—3.15	.003	49.82	0.24
Smoking current	No Tool	5 (16780)	1.19	1.07—3.53	.030	85.56	0.33
	Tool	9 (1045)	0.83	0.60—1.15	.265	17.36	0.04
Smoking current/history	No Tool	8 (24122)	1.41	1.04—1.92	.029	76.07	0.12
	Tool	13 (1691)	0.92	0.73—1.15	.458	0	0
Pre-Operative (Continuous)							
Age (years)	No Tool	8 (3118)	3.11*	1.50—4.72	<.001	51.30	2.31
	Tool	20 (6185)	4.52*	2.95—6.09	<.001	82.93	9.67
BMI	No Tool		Insufficie	nt Data			
	Tool	4 (776)	0.023*	-0.6—0.65	.653	15.02	0.07
Cognition: All tests	No Tool		Insufficie	nt Data			
	Tool	9 (887)	-0.58†	-0.78— -0.37	<.001	34.11	0.03
Cognition: MMSE only	No Tool		Insufficie	nt Data			
	Tool	7 (621)	1.14*	-1.91— -0.36	.004	77.72	0.68
Depression GDS	No Tool		Insufficie	nt Data			
	Tool	2 (233)	0.75*	-0.15—1.65	.101	0	0
Education (years)	No Tool		Insufficie	nt Data			
	Tool	6 (665)	-0.93*	-1.65—-0.20	.012	19.31	0.16
EuroSCORE	No Tool	3 (1058)	3.06*	0.28—5.83	0.31	95.87	5.71

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Variable	Delirium Diagnosis	k (n)	Pooled Es OR/MD*/	stimate 95%CI	p value	Heter I <sup>2</sup>	ogeneity Tau <sup>2</sup>
			SMD†				
	Tool	7 (10141)	0.65*	0.14—1.16	.012	89.23	0.37
LVEF (%)	No Tool	4 (2518)	1.91*	-1.94—5.77	.330	91.24	13.83
	Tool	7 (790)	0.82*	-1.24—2.89	.435	57.05	4.24
Intra-Operative (Continuous)							
ACC time (mins)	No Tool	7 (3026)	9.88*	-0.52—20.29	.063	94.19	176.11
	Tool	9 (4462)	3.61*	-0.97—8.18	.123	75.77	34.07
CPB time (mins)	No Tool	8 (7693)	4.98*	2.33—7.63	<.001	0	0
	Tool	13 (4719)	7.91*	2.37—13.45	.005	60.91	52.60
Duration of surgery (mins)	No Tool		Insufficie	nt Data			
	Tool	12 (1851)	19.66*	7.18—32.14	.002	77.61	342.16
Intubation time (hours)	No Tool	3 (2194)	7.391*	1.78—13.00	.010	94.02	22.48
	Tool	8 (4499)	6.62*	1.25—12.00	.016	98.50	57.31
Number of grafts	No Tool	3 (1863)	0.06*	-0.27—0.38	.738	58.79	0.05
	Tool	5 (868)	0.15*	0.04—0.27	.009	0	0
Post-Operative (Categorical)							
Arrhythmia, incl. AF	No Tool	7 (4423)	4.26	2.16—8.40	<.001	82.46	0.65
	Tool	9 (4386)	2.98	1.93—4.61	<.001	52.46	0.20
Post-Operative (Continuous)							
LOS in ICU (days)	No Tool	4 (2390)	3.39*	-0.16—6.94	.061	99.04	12.59
	Tool	10 (4787)	1.69*	1.06—2.31	<.001	94.03	0.86

Note: "Delirium Diagnosis" indicates analyses conducted by categorization of diagnostic method, where "No Tool" represents studies that did not utilize a specific instrument and "Tool" represents studies utilizing a standardized instrument e.g. Confusion Assessment Method (CAM) or the Delirium Rating Scale (DRS) to inform the reference standard. ACC= aortic cross-clamp, AF= atrial fibrillation, BMI= body mass index, CI= cognitive index score, CPB= cardiopulmonary bypass, CVA= cerebrovascular attack, GDS= geriatric depression scale, k= number of estimates (number of studies), LOS= length of stay, LVEF= left ventricular ejection fraction, MD= mean difference, MI= myocardial infarction, MMSE= mini mental state examination, n= pooled sample size, OR= odds ratio, PVD= peripheral vascular disease, SMD= standardised mean difference and TIA= transient ischemic attack. Symbols following pooled estimates denote different effect sizes: indicating OR (no symbol), MD\* and SMD†.

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
51	Al Tmimi, 2016	Delirium: CAM or CAM-ICU	Delirium: Positive CAM/CAM-ICU score (Y)
52	Baba, 2007	Cognition: HDS, Kana pick-out test, digit symbol, digit span (forward & backward)	Cognition: 20% method
53	Boodhwani, 2006	Cognition: Total learning free recall, consistent long-term retrieval, long-term retrieval, long- term storage, delayed recall, digit span (forward & backward), trails A & B, grooved pegboard, symbol digit modalities, RAVLT, Buschke selective reminding, WMS-III/mental control	Cognition: 0.5 SD method
54	Braekken, 1998	Cognition: WAIS vocabulary, WAIS picture completion, RCPM, CVLT-L, CVLT-S, CVLT-L, serial digit learning, WMS drawing, trails A & B, letter cancellation task, WAIS	Cognition: 1 SD method

## Table S8. Study specific information regarding instruments utilized and method of classification/diagnosis utilized.

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium	
No.			(Standardized Delirium Measurement Tool: Y/N)	
		digit symbol, computerized RT, COWAT, grooved pegboard		
55	Bucerius, 2005	Delirium: APA guidelines	Delirium: According to APA guidelines (N)	
56	Caldas, 2019	Delirium: CAM-ICU	Delirium: Positive CAM-ICU score (Y)	
57	Chen, 2017	Delirium: CAM-ICU	Delirium: Positive CAM-ICU score (Y)	
58	Christiansen, 2016	Cognition: VVLT, CST, stroop test, LDCT	Cognition: Decline of $\geq 20\%$ in $\geq 2$ tests	
59	Coffey, 1983	Delirium: DSM-III criteria	Delirium: DSM-III diagnostic criteria (N)	
60	Colak, 2015	Cognition: MMSE, color trail test, grooved pegboard	Cognition: Miscellaneous	
		Delirium: DSS	Delirium: Patient met criteria specific to study (N)	
61	Cumurcu, 2008	Delirium: DRS (for severity), DSM-IV-TR criteria, MMSE	Delirium: DSM-IV-TR diagnostic criteria (N)	

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
62	de Tournay-Jette, 2011	Cognition: MMSE (pre-screen, excluded if <24 pre-surgery), logical memory subtest (of the Rivermead battery), RAVLT, digit symbol, trails A & B, stroop test, verbal fluency test	Cognition: 1 SD method
63	Dieleman, 2009	Cognition: RAVLT-L, RAVLT-R, grooved pegboard, trails A & B, Sternberg memory comparison, line orientation test, stroop test, continuous performance task, self-ordering tasks, visuospatial working memory, symbol digit modalities	Cognition: RCI method
64	Djaiani, 2003	Cognition: Randt short story, WAIS digit span, WMS figural memory, WAIS digit symbol, Trails B, RAVLT	Cognition: 1 SD method
65	Dong, 2014	Cognition: 12 neuropsychological tests used to assess cognitive functions including attention, memory and executive function	Cognition: RCI method

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
		Delirium: CAM-ICU	Delirium: Positive CAM-ICU score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
		Delirium: DSM-III-R	Delirium: DSM-III-R diagnostic criteria (N)
66	Eriksson, 2002	Delirium: CAM and OBS scale	Delirium: Positive CAM score and fulfilled DSM-IV criteria (Y)
67	Goto, 2000	Cognition: HDS	Cognition: Cutoff method
68	Gottesman, 2010	Delirium: DSS	Delirium: Charts reviewed for delirium in those with neurologic injury (N)
69	Hall, 1999	Cognition: Trails A & B, digit span (forward & backward), COWAT	Cognition: Z-score method
70	Harmon, 2004	Cognition: RAVLT, trails A & B, grooved pegboard, COWAT, digit symbol	Cognition: RCI method

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)
		Delirium: DSM-III-R, MMSE	Delirium: Diagnosis based on the DSM-III-R criteria and the MMSE (N)
71	Harmon, 2005	Cognition: RAVLT, trails A & B, grooved pegboard, COWAT, digit symbol	Cognition: RCI method
		Delirium: DSM-III-R, MMSE	Delirium: Diagnosis based on the DSM-III-R criteria and the MMSE (N)
		Delirium: ICDSC	Delirium: ICDSC score $\geq 4$ (Y)
72	Humphreys, 2016	Delirium: DSI, SPMSQ	Delirium: Positive DSI score (had any one of the critical symptoms of delirium: disorientation, disturbance of consciousness, or perceptual disturbance) (Y)
73	Kadoi, 2001	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
74	Kadoi, 2002	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
75	Kadoi, 2003	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
76	Kadoi, 2005	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
77	Kadoi, 2007	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
79	Kadoi, 2011 (a)	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
78	Kadoi, 2011 (b)	Cognition: MMSE, RAVLT, trails A & B, digit span (forward), grooved pegboard	Cognition: 1 SD method
80	Kazmierski, 2014 (a)	Cognition: MoCA, trails B	Cognition: Cutoff method

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
		Delirium: CAM or CAM-ICU, RASS	Delirium: If RASS was above –4 (–3 through +4), assessment with the CAM-ICU was administered (Y)
81	Kazmierski, 2014 (b)	Delirium: CAM-ICU, MDAS (for severity)	Delirium: Positive CAM-ICU score (Feature 1 and Feature 2 and either Feature 3 or 4 are present) (Y)
82	Kazmierski, 2014 (c)	Delirium: CAM-ICU	Delirium: If RASS was above –4 (–3 through +4), assessment with the CAM-ICU was administered (Y)
83	Khan, 2014	Delirium: DSM-IV	Delirium: Diagnosed using DSM-IV criteria (N)
84	Khatri, 1999	Cognition: Randt short story, WAIS-R digit span, WAIS-R digit symbol, trails B, figural memory	Cognition: 20% method
85	Kok, 2017	Cognition: CogState brief computerized test battery (detection task, identification task, one card learning task and one back task)	Cognition: RCI method

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
86	Kumpaitiene, 2019	Cognition: MMSE, RAVLT, WAIS digit span, WAIS digit symbol, Shulte table	Cognition: Pre-post change of >2 points in combined studentized score, or >2 points in ≥2 individual studentized test scores.
87	Lachmann, 2018	Motor choice RT, grooved pegboard, Trails A & B, symbol digit modalities, stroop test, continuous performance task, RAVLT, self- ordering tasks, visual/spatial working memory, Sternberg memory comparison, line orientation	Cognition: Decrease of ≥20% on ≥3 tests
88	Leenders, 2018	Delirium: CAM, CAM-ICU, multidisciplinary consultation	Delirium: Administration of haloperidol in addition to positive CAM or CAM-ICU score and multidisciplinary consultation (Y)
89	Li, 2015	Delirium: CAM	Delirium: Positive CAM score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
90	Liu, 2009	Cognition: WMS mental control, WMS visual retention, WMS paired-associate verbal learning, digit span (forward and backward),	Cognition: RCI method

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)
		WAIS-R digit symbol, trails A, grooved	
		pegboard (dom & non-dom)	
91	Loponen, 2008	Delirium: DSS (clinically diagnosed)	Delirium: Clinically diagnosed with requirement that temporary medication, i.e. diazepam or haloperidol, was needed to sedate the delirious patient (N)
92	Mardani, 2012	Delirium: DSM-IV, MMSE	Delirium: DSM-IV criteria interviews conducted on patients with a MMSE score $\leq 23$ (N)
93	Mariscalco, 2012	Delirium: CAM-ICU	Delirium: At least 2 positive assessments on CAM- ICU (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
94	Martin, 2010	Delirium: STS	Delirium: Defined according to STS definition (N)
95	Martin, 2012	Delirium: STS	Delirium: Defined according to STS definition (N)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
96	Mathew, 2006	Cognition: Randt short story, WMS modified visual reproduction test, WAIS-R digit span, WAIS-R digit symbol, trails B	Cognition: 1 SD method (domain)
97	Mathew, 2007	Cognition: Randt short story, WMS modified visual reproduction test, WAIS-R digit span, WAIS-R digit symbol, trails B	Cognition: 1 SD method (domain)
98	Miyazaki, 2011	Delirium: DSM-IV	Delirium: Diagnosed according to DSM-IV criteria or administering antipsychotic agents by reviewing medical records during the ICU stay (N)
99	Mu, 2010	Delirium: CAM-ICU, RASS	Delirium: If RASS was above –4 (–3 through +4), assessment with the CAM-ICU was administered (4-step algorithm) (Y)
100	Mu, 2013	Cognition: Trails A, grooved pegboard (dom & non-dom), the WMS-Chinese edn. of the mental control subtest, digit span subtest (forward & backward), visual retention subtest,	Cognition: 1 SD method (preop) / RCI method

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)
		paired associate verbal learning subtest, digit symbol subtest	
101	Newman, 1987	Cognition: RAVLT, non-verbal recognition memory test (computer-administered), Trails A & B, WAIS block design, Purdue Pegboard (left, right, and both hands), letter cancellation test, symbol digit replacement (computer- based), choice RT (computer-based)	Cognition: Decrease of ≥1SD in >3 tests
102	Nikolic, 2012	Delirium: CAM	Delirium: Positive CAM score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
103	Norkiene, 2007	Delirium: DSM-IV	Delirium: Clinician diagnosis according to DSM-IV criteria (N)
104	Norkiene, 2011	Cognition: MMSE, RAVLT, trails A & B, digit span, digit symbol, cube drawing	Cognition: 1 SD method
		Delirium: DSM-IV	Delirium: Defined according to DSM-IV criteria (N)

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)
105	Oh, 2008	Cognition: MMSE, trails A, grooved pegboard	Cognition: 20% method
106	Oh, 2017	Delirium: DSS (psychiatric consultation & DSM- IV)	Delirium: Diagnosed by psychiatric consultation according to DSM-IV criteria (N)
107	Oldham, 2015	Cognition: CDR, MMSE, digit span, HVLT, WMS-IV, progressive digit sequencing, three word fluency tasks, NAB mazes subtest, trails A & B, digit symbol	Cognition: Cutoff method, 1 SD method
		Delirium: aDST, CAM, DI, MMSE	Delirium: Determined based on CAM (Y)
108	Oldham, 2019	Delirium: CAM, MMSE, abbreviated digit span test, DI	Delirium: Psychiatrist diagnosis based on CAM, MMSE, digit span test and delirium index (Y)
109	Omiya, 2015	Delirium: DRS-R-98	Delirium: DRS-R-98 score $\geq 8$ (Y)
110	Otomo, 2013	Delirium: DSM-IV, DRS	Delirium: Diagnosed according to DSM-IV criteria & DRS score (Y)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
111	Palmbergen, 2012	Delirium: DOS scale, confirmed by geriatrician or internist	Delirium: DOS scale for screening. If suspected, confirmed by geriatrician or internist (Y)
112	Plaschke, 2010	Delirium: CAM-ICU (German), RASS	Delirium: Positive CAM-ICU score (Y)
113	Reents, 2002	Cognition: d2-letter cancellation test, trails B, Benton's visual retention test, WAIS block design, WAIS digit span	Cognition: 1 SD method
		Delirium: DSM-IV	Delirium: Defined according to DSM-IV criteria (N)
114	Restrepo, 2002	Cognition: Trails B, oral and written naming test, oral reading tests, line cancellation, Bells tests	Cognition: Z-score method
115	Ringaitiene, 2015	Delirium: CAM-ICU	Delirium: Positive CAM-ICU score (Y)
116	Robson, 2000	Cognition: RAVLT, trails A & B, PASAT, grooved pegboard, COWAT, NART, block design, object assembly test, digit symbol, picture completion test	Cognition: 1 SD method (<20% tests), 0.5 SD method (<20% tests)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
117	Rodriguez, 2010	Cognition: Group 1: RAVLT, trails A & B, grooved pegboard, symbol digit modalities, WAIS-R digit span, WMS mental control, letter (FAS test), category fluency (animal naming), finger tapping; Group 2: RAVLT, trails A & B, grooved pegboard, symbol digit modalities, WAIS-R digit span, verbal fluency (FAS test), categories (animal naming)	Cognition: Z-score method
118	Rolfson, 1999 (a)	Delirium: CAM, MMSE, DSM-III-R	Delirium: Diagnosed according to DSM-III-R criteria, based on results from standardized measures (e.g. CAM) and consultation with nurses, family members and hospital records (Y)
119	Rolfson, 1999 (b)	Delirium: DSM-III-R on clinical grounds (CAM, CAM-MD, CAM-RN, MMSE, clock drawing test, MD chart review, RN chart review - used to determine clinical diagnosis)	Delirium: Clinically diagnosed according to DSM- III-R criteria, based on results from standardized measures (Y)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
120	Royse, 2000	Cognition: Recall (short-term & delayed), COWAT, trails A & B, grooved pegboard (dom & non-dom), digit symbol, digit span (forward & backward)	Cognition: 20% method
121	Royse, 2011	Cognition: Trails A & B, COWAT, stroop test, letter cancellation, grooved pegboard (dom & non-dom), RAVLT, digit span (forward & backward), symbol digit modalities	Cognition: 1 SD method (<20% tests)
		Delirium: CAM	Delirium: Positive CAM score (Y)
122	Rudolph, 2005	Delirium: CAM, digit span, DSI, MDAS, MMSE	Delirium: Positive CAM score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
123	Rudolph, 2006	Delirium: CAM (CAM-ICU for postoperatively intubated patients), digit span, DSI, MDAS, MMSE	Delirium: Positive CAM score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
124	Rudolph, 2009	Delirium: CAM, digit span, DSI, MDAS, MMSE	Delirium: Positive CAM score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
125	Sahan, 2018	Cognition: WMS logical memory, clock drawing test, word list generation test, digit span, visuomotor spatial skills test	Cognition: 1 SD method (≥2 tests)
6	Santos, 2004	Delirium: DSM-IV	Delirium: Diagnosed by geriatrician based on DSM- IV criteria, in addition to notes from nurses and physicians (N)
126	Scott, 2002	Cognition: WMS-R logical memory (I & II), altered form of WMS-R digit span, trails A & B, COWAT	Cognition: 1 SD method (<20% tests), 1 SD method
127	Sevuk, 2015	Delirium: DRS-R-98 (for severity), ICDSC	Delirium: ICDSC score $\geq 4$ (Y)
128	Siepe, 2011	Delirium: MMSE, psychologist assessment	Delirium: 10 point drop or more on MMSE from pre-op and a positive assessment by a psychologist (N)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
129	Silbert, 2006	Cognition: CERAD AVLT, digit symbol, Trails A & B, COWAT, semantic fluency test, grooved pegboard test (dom & non-dom)	Cognition: 1 SD method and 20% method (≥2 tests)
130	Silbert, 2008	Cognition: CERAD AVLT, Digit symbol, Trails A & B, COWAT, semantic fluency test, grooved pegboard test (dom & non-dom)	Cognition: 1 SD method (≥2 tests)
131	Slater, 2009	Cognition: MMSE, Trails A & B, HVLT (trials 1, 2, 3, B & C), grooved pegboard (dom & non- dom), stroop test (part C & CW)	Cognition: 1 SD method (<20% tests)
		Delirium: DRS	Delirium: Based on DRS (Y)
132	Smith, 1986	Cognition: WAIS vocab and picture completion subtests, RAVLT, block design, grooved pegboard, trails A & B, letter cancellation, digit symbol replacement, two-choice RT	Cognition: 1 SD method

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
133	Smith, 2000	Cognition: RAVLT, Rey auditory nonverbal memory, Trails A & B, letter cancellation, symbol-digit replacement, visual RT, grooved pegboard (dom & non-dom), finger tapping (dom & non-dom)	Cognition: 20% method (≥2 tests)
134	Stump, 1996	Cognition: Trails A & B, grooved pegboard (dom & non-dom), finger tapping (dom & non-dom), symbol digit, letter cancellation, visual RT, verbal and nonverbal memory	Cognition: 20% method (≥2 tests)
135	Subramaniam, 2019	Delirium: CAM, CAM-ICU	Delirium: Positive CAM or CAM-ICU score (Y)
136	Suksompong, 2002	Cognition: Thai Mental State Exam	Cognition: Miscellaneous
137	Swaminathan, 2002	Cognition: Randt short story (immediate & delay), digit symbol, trails B, digit span (forward & backward), figural memory (immediate & delayed)	Cognition: 1 SD method (domain)

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (Standardized Delirium Measurement Tool: Y/N)
138	Sylivris, 1998	Cognition: WAIS-R general information questionnaire, digit span, digit symbol, RAVLT, COWAT	Cognition: Miscellaneous
139	Tagarakis, 2007	Delirium: DRS	Delirium: Based on DRS, which was performed on patients suspected to develop delirium (Y)
140	Tamura, 2019	Delirium: ICDSC	Delirium: ICDSC >3
141	Toeg, 2013	Cognition: Buschke selective reminding or RAVLT, WAIS-R digit span, finger tapping task, letter and category fluency, trails A & B, grooved pegboard, symbol digit modalities	Cognition: 1 SD method (domain)
142	Trubnikova, 2014	Cognition: Complex visuomotor reaction (reaction time, number of errors), functional mobility of nervous processes and performance of brain responses to feedback (reaction time, number of errors, missed signals), Bourdons test, visual short-term memory tests	Cognition: 20% method

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)
		(memorisation of 10 numbers, 10 words, 10 nonsense syllables)	
143	Tully, 2010	Delirium: DSI, DSM-IV-TR, SPMSQ	Delirium: Classification based on DSM-IV-TR criteria. Evidence of perceptual disturbance and/or language disturbance was requisite for a delirium diagnosis. Neurology assessments, SPMSQ results and medical notes also evaluated. (N)
144	van Dijk, 2004	Cognition: RAVLT-L, RAVLT-R, grooved pegboard, trails A & B, Sternberg memory comparison, line orientation test, stroop test	Cognition: 20% method
145	Yilmaz, 2016	Delirium: CAM-ICU	Delirium: Positive CAM-ICU score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)
146	Zhang, 2015	Delirium: CAM-ICU, RASS	Delirium: Positive CAM-ICU score (Features 1 and 2 are present and either Feature 3 or 4 is present) (Y)

Reference	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium
No.			(Standardized Delirium Measurement Tool: Y/N)

Note. see Supplementary Table 9 for glossary of instrument acronyms

# Table S9. Glossary of abbreviations.

	Cognitive Impairment		
AVLT	Auditory Verbal Learning Test		
CDR	Clinical Dementia Rating scale		
CERAD	The Consortium to Establish a Registry for Alzheimer's Disease		
COWAT	Controlled Oral Word Association Test		
CST	Concept Shifting Test		
CVLT	California Verbal Learning Test		
Digit symbol	Digit Symbol Substitution Task		
HDS	Hasegawa Dementia Scale		
HVLT	Hopkins Verbal Learning Test		
LDCT	Letter-Digit Coding Test		
MMSE	Mini Mental State Examination		
MoCA	Montreal Cognitive Assessment		
NAB	Neuropsychological Assessment Battery		
NART	National Adult Reading Test		
PASAT	Paced Auditory Serial Addition Task		
Randt short story	Randt Memory Test Short-Story Module		
RAVLT	Rey Auditory Verbal Learning Test		
RAVLT-L	Rey Auditory-Verbal Learning – Learning Trial		
RAVLT-R	Rey Auditory-Verbal Learning – Recognition Trial		
RCPM	Raven Coloured Progressive Matrices		
RT	Reaction Time		
Stroop test	Stroop Colour Word Interference Test		
Trails A & B	Halstead-Reitan Trail-making tests A & B		

VVLT	Visual Verbal Learning Test
WAIS	Wechsler Adult Intelligence Scale
WMS	Wechsler Memory Scale
	Delirium
aDST	abbreviated Digit Span Test
APA	American Psychiatric Association
CAM	Confusion Assessment Method
CAM-ICU	Confusion Assessment Method for the ICU
DI	Delirium Index
DOS	Delirium Observation Screening scale
DRS	Delirium Rating Scale
DRS-R-98	Delirium Rating Scale Revised-98
DSI	Delirium Symptom Interview
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders 3 <sup>rd</sup> ed., Revised.
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 4 <sup>th</sup> ed.
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders 4 <sup>th</sup> ed., Text Revision
DSS	Definition that is specific to the study
ICDSC	The Intensive Care Delirium Screening Checklist
MDAS	Memorial Delirium Assessment Scale
MMSE	Mini Mental State Examination
OBS	Organic Brain Syndrome scale
RASS	The Richmond Agitation Sedation Scale
SPMSQ	Short Portable Mental Status Questionnaire
STS	Accordance with Society of Thoracic Surgeons

## Figure S1. Forest plots for delirium post-CABG analyses.

Variable	Forest Plot						
Pre-Operative (Categorical)							
Alcoholism	Study name		Statistic	cs for e	ach stud	Y	Odds ratio and 95% CI
		Odds I					
		ratio	limit	limit	Z-Value	p-Value	
	Dong, 2014	1.057	0.362	3.084	0.101	0.919	
	Humphreys, 2016	1.280	0.390	4.206	0.407	0.684	│ │ <del>│ <mark>│ </mark>┃ <mark>┃</mark> </del>
	Loponen, 2008	8.235		95.421	1.687	0.092	
	Mu, 2010	0.557	0.265	1.171	-1.543		
	Ringaitiene, 2015	1.487		31.270	0.256		
	Rolfson, 1999a	0.375	0.038	3.699	-0.840		
		0.899	0.500	1.615	-0.357	0.721	
							0.1 0.2 0.5 1 2 5 1
Arrhythmia, incl. AF							
Arrhythmia, incl. AF	Study name			05/15	ach study		Odds ratio and 95% Cl
		Odds ratio	Lower limit	Upper	Z-Value	p-Value	
	Caldas, 2019	0.719	0.075	6.915	-0.286	0.775	
	Coffey, 1983	0.629	0.149	2.652	-0.632	0.528	
	Dong, 2014	1.310	0.519	3.303	0.571	0.568	
	Eriksson, 2002	0.258	0.013	5.012	-0.895	0.371	
	Gottesman, 2010	2.363	1.647	3.392	4.665	0.000	
	Kazmierski, 2014a	2.361	0.597	9.343	1.224	0.221	
	Kazmierski, 2014b	2.778		15.517	1.164	0.244	
	Mardani, 2012 Martin, 2010	4.519 1.883	1.522	19.614 2.330	2.014 5.824	0.044	
	Martin, 2012	2.070	1.575	2.720	5.218	0.000	
	Miyazaki, 2011	2.728	1.283	5.799	2.608	0.009	
	Mu, 2010	1.271	0.703	2.299	0.794	0.427	
	Nikolic, 2012	1.933	0.946	3.951	1.808	0.071	
	Santana Santos, 2004			14.872	1.664	0.096	
	Zhang, 2015	5.103 2.068	2.535	10.269	4.567	0.000	
		2.000	1.700	2.314	1.211	0.000	0.1 0.2 0.5 1 2 5 1
							0.1 0.2 0.5 1 2 5 1
							Favours A Favours B
3MI >28 (including >30)	Study name	Stati	istics for	each st	udy		Odds ratio and 95% CI
	Odd rati		r Uppe limi		ue p-Val	ue	
	Caldas, 2019 1.3	16 0.29	9 5.7	38 0.3	364 0.7	16	
	Chen, 2017 1.3			94 0.7		460	│ │ <u>─┼<u>■</u>┼── │</u>
	Martin, 2010 0.7					003	
	Norkeine, 2007 1.2	44 0.65	55 2.30	64 0.6		505	
	Royse, 2011 2.8	00 1.16	6.7	52 2.2		022	▏
	Rudolph, 2005 1.7	50 0.44	19 6.8	25 0.8	306 0.4	120	│ ┼┼┲┼─┼─
	Zhang, 2015 0.6	95 0.26	56 1.8	15 -0.7		457	
	1.1	58 0.74	14 1.8	0.0	649 0.5	516	
	0.000						

BMI ≥30 only	Study name		Statist	ics for	each st	udy	-				Odds	ratio	and 9	5% CI	_
		Odds ratio	Lower limit		Z-Va	lue	p-Val	ue							
	Caldas, 2019	1.316	0.299	5.78	3 0.3	364	0.7	16	Ĩ		-	-	-	-+	Ĩ
	Chen, 2017	1.397	0.575	3.39	4 0.	738	0.4	60			3	-			
	Norkeine, 2007	1.244	0.655	2.36	4 0.	667	0.5	05				-	-		
	Royse, 2011	2.800	1.161	6.75	2 2.	293	0.0	22					-		
	Rudolph, 2005	1.750	0.449	6.82	5 0.	806	0.4	20			1		-		-
		1.573	1.045	2.36	3 2.	172	0.0	30					-		
									0.1	0.2	0.5	1	2	5	10
Cognitive Impairment	Study name		Stati	stics fo	reach	study	у_			4	Odds r	atio a	and 95	% CI	
		Odds ratio	s Lowe			alue	p-Va	alue							
	Leenders, 2018	4.08	1 1.44	46 11.5	20 2	2.656	0.	800	1	- T	1	- 1	+		
	Oldham, 2018	3.00	0 1.1:	23 8.0	13 🕻	2.192	0.	028					-		_
	Kazmierski, 2014a	a 7.61	9 2.93	27 19.8	32 4	4.160	0.	000						-	
	Oldham, 2015	6.11	1 1.0	56 35.3	63 💈	2.021	0	.043							
	Rudolph, 2005	4.00	0 0.9	81 16.3	11 .	1.933	0.	053				ŀ	-		
	Zhang, 2015	4.44	6 1.6	76 11.7	97 2	2.997	0.	.003					-		
	Rolfson, 1999b	2.31	1 0.7	52 7.1	06	1.462	0	.144				-			-0
		4.17	0 2.74	46 6.3	32 (	5.700	0.	000							•
									0.1	0.2	0.5	1	2	5	10
	Study name			Statistic	s for e	ach s	study				Odd	s rati	oand	95% CI	
			Odds L ratio		Z-Value		per mit	p-Valu	e						
	Oldham, 2018		3.984	1.158	2.19	3 13	.705	0.02	8	- Î	T	1	1-		
Depression	Santana Santos, 2	2004	1.242	0.553	0.52	5 2	.787	0.60	0			_		- 1	
L	Tully, 2010		3.490	1.477	2.85	0 8	.245	0.00	4				_		_
	Rolfson, 1999a		4.846	0.408	1.25	0 57	.544	0.21	1		į	+	-	-	)
			2.493	1.291	2.72	2 4	.811	0.00	6						
										0.1	0.2	0.5	1 :	2 5	10

Diabetes	Study name		Statis	tics for e	ach study		Odds ratio and 95% Cl
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
	Caldas, 2019	2.333	0.746	7.301	1.456	0.145	
	Chen, 2017	1.421	0.690		0.954		
	Leenders, 2018 Dong, 2014	1.456	0.722		1.050	0.294	
	Eriksson, 2002	1.889	0.394		0.795	0.427	
	Gottesman, 2010	1.285	1.011		2.050	0.040	
	Bucerius, 2005	1.616	1.390		6.239	0.000	
	Coffey, 1983 Humphreys, 2016	1.564	0.597		0.910	0.363	
	Kazmierski, 2014a	1.154	0.517			0.727	
	Kazmierski, 2014b	1.000	0.363		0.000	1.000	
	Khan, 2014 Loponen, 2008	1.237	0.872			0.234 0.162	
	Mardani, 2012	0.661	0.143			0.596	
	Mariscalco, 2012	1.398	0.910		1.529	0.126	
	Martin, 2010 Martin, 2012	1.481	1.299		5.869 4.687	0.000	
	Miyazaki, 2011	1.539	1.021		2.059	0.039	
	Mu, 2010	1.767	1.041		2.109	0.035	
	Nikalic, 2012 Narkeine, 2007	1.997	1.152		2.465	0.014	
	Omiya, 2015	0.354	0.036			0.372	
	Otomo, 2013	1.555	0.548	4.415	0.830	0.407	
	Ringaitiene, 2015	1.882	0.416		0.821	0.412	
	Rudolph, 2005 Santana Santos, 2004	2.286	0.586		1.191 1.224	0.234	
	Sevuk, 2015	1.124	0.611				
	Tully, 2010	0.718	0.345			0.376	
	Yilmaz, 2016 Zhang, 2015	0.820	0.284			0.714	
	Zhang, 2015	1.491	1.390			0.000	
							0.1 0.2 0.5 1 2 5 10
Dyslipidemia/Hyperlipidemia	Study name			Statisti	cs for ea	ach study	y Odds ratio and 95% CI
			odds I ratio	Lower limit	Upper limit	7-Value	p-Value
	0.11 0010						
	Caldas, 2019		0.395	0.126	1.240	-1.592	
	Dong, 2014		1.399	0.640	3.055	0.842	
	Coffey, 1983		0.212	0.074	0.606	-2.898	
	Humphreys, 2016		2.560	0.909	7.206	1.780	
	Loponen, 2008		1.066	0.368	3.085	0.118	
	Mariscalco, 2012		0.630	0.411	0.965		
	Mu, 2010		1.028	0.615	1.720	0.107	
	Omiya, 2015		4.000	0.217		0.933	
	Otomo, 2013		0.461	0.162	1.314	-1.449	
	Rudolph, 2005		1.474			0.304	
	Santana Santos, 200		0.639	0.332			
	Sevuk, 2015		1.442	0.784	2.652	1.176	
	Tully, 2010		1.481	0.658	3.336	0.948	
			0.890	0.633	1.251	-0.072	
							0.1 0.2 0.5 1 2 5 10
Education>12years/high school	Study name			Statisti	cs for ea	ach study	Odds ratio and 95% Cl
	864		dds L atio	ower limit	Upper limit	Z-Value	p-Value
	0.0017						
		C	).568	0.211	1.535	-1.115	
	Chen, 2017					0 407	
	Oldham, 2018		). <b>77</b> 9	0.291	2.086	-0.497	
	Oldham, 2018 Rudolph, 2006	1	).779 1. <mark>000</mark>	0.291 0.416	2.086 2.405	0.000	1.000
	Oldham, 2018	1					1.000
	Oldham, 2018 Rudolph, 2006	1 4 C	1.000	0.416 0.134	2.405 1.009	0.000 -1.942	1.000
	Oldham, 2018 Rudolph, 2006	1 4 C	1.000 ).368	0.416	2.405	0.000 -1.942	1.000 0.052 0.088
	Oldham, 2018 Rudolph, 2006	1 4 C	1.000 ).368	0.416 0.134	2.405 1.009	0.000 -1.942	1.000

	Study name		Statist	tics for ea	ch study		Odds ratio and 95% CI
		Odds ratio		Upper limit	Z-Value	n Value	
						10.000000	
	Caldas, 2019	2.368		11.871	1.048	0.294	
	Chen, 2017 Dong, 2014	4.440		10.987 3.179	3.225 0.919	0.001	
	Eriksson, 2002	1.800		7.712	0.792	0.428	
	Gottesman, 2010	1.391		1.847	2.285	0.022	
	Coffey, 1983	1.649	0.836	3.255	1.442	0.149	
	Humphreys, 2016	0.750		1.505	-0.810	0.418	
	Kazmierski, 2014a	1.285		3.687	0.467	0.641	
	Khan, 2014	1.683		2.410	2.844	0.004	
	Loponen, 2008 Mardani, 2012	1.593		4.365	0.905 4.051	0.365	
	Mariscalco, 2012	0.671		1.037	-1.797	0.072	
	Martin, 2010	1.511		1.754	5.434	0.000	
	Martin, 2012	1.706		2.100	5.040	0.000	
	Miyazaki, 2011	2.705	5 1.526	4.796	3.406	0.001	
	Mu, 2010	1.395		2.379	1.221	0.222	│ │ │ <del>┼■┼</del> │
	Nikolic 2012	2.240		6.548	1.474	0.141	
	Norkeine, 2007	0.968		2.040	-0.094	0.925	
	Omiya, 2015 Otomo, 2013	0.850		5.366 1.447	-0.173 -1.294	0.863	
	Ringaitiene, 2015	0.48		1.44/	-0.088	0.196	
	Rudolph, 2005	2.600		15.177	1.062	0.288	
	Santana Santos, 200			4.451	2.268	0.023	
	Sevuk, 2015	0.867	0.424	1.773	-0.392	0.895	
	Tully, 2010	0.811		1.631	-0.587	0.557	
	Yilmaz, 2016	0.650		1.986	-0.756	0.450	
	Zhang, 2015	1.319		2.283	0.989	0.323	
Sex (male)	<u>Study name</u>		atistics for wer Uppe		dy		Odds ratio and 95% CI
				it Z-Valu	ue p-Valu	ə	
	Caldes, 2019	1.026	0.281 3.7	47 0.03	0.96	9	
	Chen, 2017	0.180	0.077 0.4	21 -3.96	0.00	о .	<del>&lt; ∎</del>
	Leerders, 2018		0.752 8.4			26.57	
	Oldham, 2018 Cumurcu, 2008		0.102 0.7 0.093 1.4				
	Dorg, 2014		0.377 2.2				
	Erikeson, 2002	0.583	0.136 2.5	06 -0.72	0.469	э	
	Gottesman 2010	0.839	0.651 1.0	79 -1.36			
						29 J	
	Al Tmimi, 2016	0.595	0.164 2.1	60 -0.78	19 0.430	0	
		0.595		60 -0.78 23 -1.33	19 0.430 15 0.183	2	
	Al Tmirni, 2016 Humphreys, 2018 Kazmiersk, 2014a Khan, 2014	0.595 0.550 0.436 1.978	0.164 2.10 0.229 1.3 0.172 1.10 1.288 3.0	60 -0.78 23 -1.33 04 -1.75 39 3.11	19 0.430 15 0.182 11 0.080	2 2 2 2	
	Al Tmimi, 2016 Humphreys, 2016 Kazmierski, 2014s Khan, 2014 Li, 2015	0.595 0.550 0.436 1.978 2.273	0.164 2.10 0.229 1.3 0.172 1.10 1.288 3.0 0.097 <mark>5</mark> 33	60 -0.78 23 -1.33 04 -1.75 09 3.11 91 0.51	19 0.430 15 0.183 11 0.080 16 0.000	0 2 2 2 2	
	Al Tmimi, 2016 Humphreys, 2016 Kazmierski, 2014s Khan, 2014 Li, 2015 Loponen, 2008	0.595 0.550 0.436 1.978 2.273 4.727	0.164 2.10 0.229 1.3 0.172 1.10 1.288 3.0 0.097 53.30 0.621 35.90	60 -0.78 23 -1.33 04 -1.75 09 3.11 91 0.51 54 1.50	9 0.430 15 0.183 11 0.080 16 0.002 10 0.610 10 0.133	0 2 2 2 3	
	Al Tmimi, 2016 Humphreys, 2016 Kazmierski, 2014s Khan, 2014 Li, 2015	0.595 0.550 0.436 1.978 2.273 4.727 0.441	0.164 2.10 0.229 1.3 0.172 1.10 1.288 3.0 0.097 <mark>5</mark> 33	60 -0.78 23 -1.33 04 -1.75 39 3.11 91 0.51 54 1.50 26 -1.29	9 0.430 15 0.183 11 0.080 16 0.003 10 0.610 10 0.133 12 0.190	0 2 2 2 2 3 8	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014s Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalca, 2012 Martin, 2010	0.595 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.095	0.164 2.10 0.229 1.3 0.172 1.10 1.286 3.0 0.097 53.30 0.621 35.90 0.128 1.5 0.543 1.4 0.937 1.2	60         -0.76           23         -1.33           04         -1.75           29         3.11           91         0.51           54         1.52           26         -1.22           81         -0.41           80         1.14	99 0.430 15 0.182 16 0.002 10 0.610 10 0.133 12 0.190 10 0.882 10 0.882 10 0.256	0 2 2 2 3 8 2 4	
	Al Tmimi, 2016 Humphreys, 2016 Kazmierski, 2014s Khan, 2014 Laponen, 2018 Mardani, 2012 Marincalco, 2012 Marin, 2010 Martin, 2012	0.595 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.095 1.123	0.164 2.10 0.229 1.3 0.172 1.10 1.286 3.0 0.097 53.30 0.621 3593 0.128 1.5 0.543 1.4 0.937 1.2 0.905 1.3	60         -0.76           23         -1.33           04         -1.75           09         3.11           91         0.51           54         1.52           26         -1.29           91         -0.41           90         1.14           90         1.14	19         0.430           15         0.182           11         0.080           16         0.002           10         0.131           12         0.190           10         0.432           12         0.190           10         0.432           10         0.433           12         0.190           10         0.256           13         0.236	2 2 2 2 3 8 2 2 4 2	
	Al Tmimi, 2016 Humphreye, 2016 Kazmierski, 2014s Kharn, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalon, 2012 Martin, 2010	0.595 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.095 1.123 0.974	0.164 2.10 0.229 1.3 0.172 1.10 1.286 3.0 0.097 53.3 0.621 3593 0.128 1.5 0.543 1.4 0.937 1.2 0.905 1.3 0.504 1.8	60         -0.75           23         -1.33           04         -1.75           39         3.11           91         0.51           54         1.50           26         -1.29           91         -0.41           90         1.14           95         1.05           82         -0.07	19         0.430           15         0.162           61         0.080           16         0.002           10         0.610           12         0.190           10         0.482           10         0.482           10         0.482           10         0.482           10         0.482           10         0.482           10         0.284           13         0.286           19         0.933	0 2 2 2 3 8 8 2 2 4 2 7	
	Al Tmimi, 2016 Humphreys, 2016 Kazmienski, 2014s Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Martiscalco, 2012 Martin, 2010 Martin, 2010 Nikelic, 2012	0.595 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.095 1.123 0.974 0.970	0.164 2.10 0.229 1.3 0.172 1.10 1.286 3.0 0.097 53.3 0.627 35.99 0.128 1.5 0.543 1.44 0.937 1.2 0.905 1.3 0.504 1.8 0.533 1.7	60         -0.75           23         -1.33           04         -1.75           39         3.11           91         0.51           54         1.50           26         -1.29           81         -0.41           80         1.14           85         1.05           862         -0.07           552         -0.10	19         0.430           15         0.162           16         0.002           10         0.610           10         0.132           12         0.190           10         0.254           10         0.254           13         0.256           13         0.256           12         0.915           12         0.915	0 2 2 2 3 8 8 2 2 4 2 2 7 9	
	Al Tmimi, 2016 Humphreye, 2016 Kazmierski, 2014s Kharn, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalon, 2012 Martin, 2010	0.595 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.095 0.974 0.970 1.956	0.164 2.10 0.229 1.3 0.172 1.10 1.286 3.0 0.097 53.3 0.621 3593 0.128 1.5 0.543 1.4 0.937 1.2 0.905 1.3 0.504 1.8	60         -0.75           23         -1.33           04         -1.75           39         3.11           91         0.51           54         1.50           26         -1.29           91         -0.41           80         1.42           80         1.46           81         -0.41           80         1.45           81         -0.62           82         -0.07           82         -0.07           89         1.50	19         0.430           15         0.182           16         0.000           16         0.000           10         0.610           10         0.133           12         0.190           10         0.622           10         0.622           10         0.226           13         0.226           12         0.919           12         0.919           13         0.226           19         0.533           12         0.919           18         0.132	0 2 2 2 3 8 8 2 2 2 4 9 2 2	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014s Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Martina, 2010 Martin, 2010 Niskiic, 2012 Norkeine, 2007 Oldham, 2015 Olonne, 2013	0.595 0.550 0.436 1.978 2.273 4.727 0.444 0.900 1.096 1.123 0.974 0.970 1.998 0.975 1.855	0.164 2.1 0.229 1.3 0.172 1.1 1.288 3.0 0.097 533 0.621 3593 0.621 3593 0.503 1.4 0.937 1.2 0.905 1.3 0.504 1.8 0.504 1.8 0.504 0.8 0.818 4.8 0.818 4.8 0.501 6.8	60         -0.75           223         -1.32           024         -1.75           039         3.11           991         0.51           554         1.52           1.52         -1.22           91         -0.41           95         1.62           91         -0.41           95         1.05           960         1.14           95         1.05           962         -0.07           962         -0.10           963         1.62           964         -0.51           974         -0.41           981         1.52           981         5.51           982         -2.77           942         0.92	III         0.430           III         0.430           III         0.000           III         0.000           III         0.000           III         0.000           III         0.000           IIII         0.000	0 2 2 0 3 3 8 2 2 4 4 2 2 7 9 9 2 2 0 8 8	
	Al Tmimi, 2016 Humphrege, 2016 Kaznierski, 2014a Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalca, 2012 Mariscalca, 2012 Marin, 2010 Niskiic, 2012 Norkeine, 2007 Oldrem, 2015 Otoma, 2013 Palmbergen, 2012	0.566 0.550 0.436 1.978 2.273 4.727 0.441 0.900 1.096 1.123 0.974 0.970 1.956 0.275 1.851 1.320	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.0 0.097 3.33 0.621 3593 0.621 3593 0.621 1.5 0.563 1.4 0.937 1.2 0.937 1.2 0.936 1.3 0.905 1.3 0.905 1.3 0.905 1.3 0.564 1.8 0.633 1.7 0.816 4.8 0.036 0.8 0.636 0.8 0.636 0.8 0.637 8.2,4	660         -0.78           223         -1.32           024         -1.75           039         3.11           910         0.55           1.50         26           926         -1.22           931         -1.22           941         -0.41           950         1.14           950         1.14           951         -0.62           862         -0.10           863         1.50           862         -0.10           862         -2.17           922         -0.82	III         0.400           IS         0.420           IS         0.433           IS         0.433           IS         0.433           IS         0.433           IS         0.433           IS         0.434	0 2 0 3 3 8 2 2 4 2 2 7 7 9 9 2 2 0 5 8 2	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014s Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalca, 2012 Martin, 2010 Mistiic, 2012 Norkeine, 2017 Oldham, 2013 Paintbergan, 2012 Ringalitiene, 2015	0.566 0.550 0.436 1.978 2.273 2.273 0.441 0.900 1.095 1.123 0.970 1.976 0.970 1.976 1.976 1.976 1.976 1.320 0.275	0.164 2.10 0.229 1.3 0.172 1.11 1.288 3.00 0.097 53.30 0.627 55.30 0.627 55.90 0.128 1.5 0.543 1.4 0.937 1.2 0.905 1.3 0.544 1.4 0.937 1.2 0.905 1.3 0.544 4.6 0.058 0.8 0.501 6.8 0.501 6.8 0.501 8.2 9 0.518 2.9	660         -0.78           223         -1.32           024         -1.75           039         3.11           910         0.55           1.55         4           910         0.51           926         -1.25           931         -1.48           940         -1.44           950         1.14           951         -0.52           952         -0.10           952         -0.10           952         -0.10           952         -0.10           952         -0.10           953         -0.52           954         -0.52           957         -0.52           951         -0.52           951         -0.52           951         -0.52           951         -0.52           952         -0.52           953         -0.52	III         0.430           III         0.000           III         0.000           III         0.000           III         0.000           0.011         0.0000           0.011	0 2 0 3 8 2 2 4 2 7 7 9 9 2 0 6 6 2 7 7	
	Al Tmimi, 2016 Humphrege, 2016 Kaznierski, 2014a Khan, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalca, 2012 Mariscalca, 2012 Marin, 2010 Niskiic, 2012 Norkeine, 2007 Oldrem, 2015 Otoma, 2013 Palmbergen, 2012	0.595 0.530 0.436 1.978 2.273 4.727 0.441 0.900 1.095 1.123 0.974 0.970 1.978 0.275 1.851 1.320 0.667 2.913	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.0 0.097 3.33 0.621 3593 0.621 3593 0.621 1.5 0.563 1.4 0.937 1.2 0.937 1.2 0.936 1.3 0.905 1.3 0.905 1.3 0.905 1.3 0.564 1.8 0.633 1.7 0.816 4.8 0.036 0.8 0.636 0.8 0.636 0.8 0.637 8.2,4	660         -0.78           223         -1.33           024         -1.75           039         3.111           931         0.51           554         1.52           54         1.52           901         1.41           995         1.05           800         1.14           995         1.05           802         -0.10           808         1.52           918         1.52           924         -0.27           928         -0.52           927         0.86           93         0.62           93         0.62           93         0.62	19         0.4308           15         0.121           16         0.000           10         0.061           10         0.061           10         0.133           12         0.191           10         0.252           12         0.191           10         0.252           12         0.919           12         0.919           13         0.252           13         0.262           13         0.262           13         0.262           13         0.513           14         0.513	0 2 0 3 3 8 2 2 4 4 2 2 5 8 2 2 7 7 7 7 7 7 7	
	Al Tmimi, 2016 Humphreys, 2016 Kazmierski, 2014s Khan, 2014 Li, 2015 Laponen, 2008 Markani, 2012 Marina, 2010 Markin, 2010 Nikelic, 2012 Norkeine, 2007 Oldham, 2015 Olonn, 2013 Palmbergen, 2015 Rudbiph, 2009	0.595 0.500 0.416 1.578 2.273 4.727 0.441 0.900 1.026 1.123 0.970 1.978 0.970 1.978 1.321 1.325 1.325 1.327 0.497 2.913	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 53.3 0.627 3590 0.628 1.5 0.540 1.44 0.550 1.44 0.550 1.44 0.550 1.3 0.550 1.	660         -0.76           223         -1.33           024         -1.75           029         3.11           191         0.51           54         1.52           64         -1.25           102         -1.22           1191         0.51           1.52         -1.22           1191         -0.41           120         -1.22           121         -0.41           122         -0.10           123         -0.10           124         -0.22           127         0.42           122         -0.12           122         -0.12           1242         -0.52           127         0.42           132         -0.52           142         -0.52           153         -0.52           154         -0.52           153         -0.52           154         -0.52           153         -0.52           154         -0.52           154         -0.52           154         -0.52           155         -0.52           154	19         0.4308           15         0.1815           15         0.1816           16         0.0001           10         0.1312           10         0.1313           12         0.1910           13         0.2523           13         0.2523           12         0.919           13         0.2523           13         0.2543           13         0.3513           13         0.3513           13         0.3513           13         0.3513           14         0.3514           15         0.3514           16         0.3514	0 2 2 0 0 3 8 2 2 2 2 2 9 9 2 2 0 0 8 8 2 2 7 7 7 8 8	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014 Khar, 2014 Li, 2015 Lopanen, 2008 Mardani, 2012 Mariscafac, 2012 Martin, 2010 Miskiic, 2012 Narleine, 2017 Oldham, 2013 Paintkargan, 2012 Ringaitiene, 2015 Rudalph, 2009 Rudalph, 2009 Santara Santos, 2004 Servak, 2015	0.595 0.535 0.436 1.978 2.273 4.777 0.441 0.900 1.095 1.123 0.970 0.970 0.970 0.970 1.955 1.320 0.667 2.913 0.297 0.659 0.725	0.164 2.10 0.229 1.3 0.172 1.11 1.288 0.00 0.097 5330 0.627 5530 0.627 5590 0.628 1.5 0.564 1.8 0.564 1.8 0.564 1.8 0.656 1.8 0.657 1.8 0.657 1.8 0.658 1.8 0.058 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.808 1.	660         -0.78           223         -1.33           024         -1.75           029         3.11           910         0.51           554         1.52           54         1.52           911         0.51           912         0.51           914         0.51           915         0.41           916         0.44           917         0.44           918         1.52           917         0.44           918         1.52           917         0.44           927         0.68           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           94         0.62           94         0.62           95         0.52           963         0.62           94         0.78	19         0.430           15         0.121           16         0.020           17         0.161           10         0.431           12         0.191           13         0.225           14         0.031           15         0.431           16         0.000           17         0.001           13         0.251           13         0.251           13         0.251           13         0.251           13         0.251           14         0.002           15         0.251           16         0.133           17         0.001           18         0.515           18         0.517           19         0.333           10         0.77           10         0.531           13         0.434	0 2 0 0 3 8 2 2 4 2 0 6 8 2 0 5 8 2 2 0 5 8 2 2 7 7 9 2 0 5 8 2 2 4 4 2 2 5 4 4 2 2 5 7 7 7 9 8 8 2 2 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014s Khan, 2014 Li, 2015 Laponen, 2008 Markani, 2012 Marisa, 2010 Martin, 2010 Miktlic, 2010 Nikklic, 2012 Norkeine, 2007 Oldham, 2015 Olonna, 2013 Palmbergan, 2012 Ringaisiene, 2015 Rudolph, 2009 Rudolph, 2009 Rudolph, 2004 Santana Santos, 2004 Senke, 2015	0.595 0.505 0.436 1.978 4.727 0.441 0.900 1.123 0.970 1.976 0.275 1.855 1.320 0.667 2.913 0.297 0.659 0.765 0.795 0.795	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 53.31 0.627 3599 0.128 1.5 0.540 1.44 0.550 1.44 0.550 1.44 0.550 1.44 0.550 1.44 0.550 1.3 0.564 1.8 0.056 0.8 0.561 6.8 0.056 6.8 0.018 4.68 0.018 4.68 0.048 2.9 0.115 74.00 0.048 0.29 0.115 74.00 0.049 0.20	660         -0.78           223         -1.33           024         -1.75           029         3.111           921         0.51           554         1.52           544         1.52           911         0.41           955         1.05           912         -0.44           955         1.05           912         -0.41           956         1.05           922         -0.07           924         -0.52           936         -0.52           930         -0.52           930         -0.52           930         -0.52           933         -0.57           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           930         -0.52           9317	19         0.4301           15         0.121           16         0.0021           10         0.611           10         0.611           10         0.611           10         0.611           10         0.611           10         0.611           10         0.611           10         0.611           12         0.919           13         0.2573           12         0.919           13         0.517           13         0.517           16         0.0021           16         0.1513           17         0.1561           13         0.4241           14         0.1513           15         0.517           16         0.1513           13         0.4241	0 2 0 0 3 8 2 2 4 2 2 0 5 8 2 2 7 7 8 8 5 4 4 4	
	Al Tmimi, 2016 Humphreys, 2016 Kazmienski, 2014s Khan, 2014 Li, 2015 Loporen, 2008 Mardani, 2012 Martin, 2010 Matin, 2010 Mikelic, 2012 Norkeine, 2007 Oldham, 2015 Oldham, 2015 Ringsidene, 2015 Rudolph, 2009 Rudolph, 2006 Santana Santos, 2004 Sewk, 2015 Taganakis, 2007 Tully, 2010	0.596 0.500 0.416 1.978 2.273 4.727 0.441 0.900 1.926 1.123 0.970 1.978 0.970 1.851 1.320 0.657 2.913 0.297 0.659 0.296 0.297 0.659 0.296 0.296 0.297	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 5330 0.627 3539 0.627 3549 0.128 1.5 0.543 1.4 0.543 1.4 0.543 1.4 0.543 1.3 0.544 1.4 0.545 1.3 0.545 1.3 0.546 1.3 0.547 1.30	660         -0.75           223         -1.33           024         -1.75           029         3.11           191         0.51           54         1.52           64         -1.22           91         0.51           54         1.52           91         0.51           926         -1.22           93         1.14           95         1.05           82         -0.10           82         -0.10           82         -0.12           82         -0.12           82         -0.12           82         -0.12           82         -0.12           82         -0.12           82         -0.12           83         0.64           84         -2.07           73         -1.41           73         -1.41           73         -1.41           74         -0.22           85         1.35	19         0.4304           15         0.1815           0.1616         0.0004           10         0.616           0.0         0.616           0.0         0.616           0.0         0.616           0.0         0.616           0.0         0.616           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.626           0.0         0.627           0.6517         0.6517           0.643         0.424           0.77         0.4512           0.424         0.170	0 2 2 0 3 3 8 2 2 7 7 9 9 2 2 5 8 8 2 2 7 7 8 8 8 2 2 8 8 8 8 8 8 8 8 8	
	Al Tmimi, 2016 Humphrege, 2016 Kaznierski, 2014a Khar, 2014 Li, 2015 Loppmen, 2008 Mardani, 2012 Mariscalca, 2012 Mariscalca, 2012 Marin, 2010 Nikikic, 2012 Norkeine, 2007 Oldham, 2015 Otoma, 2013 Palmbergen, 2015 Rudalph, 2006 Santana Santos, 2004 Senak, 2015 Taganakis, 2007 Tally 2010 Yilimaz, 2016	0.596 0.500 0.436 1.378 2.273 4.727 0.441 0.900 1.096 1.123 0.970 1.956 0.275 1.856 0.275 1.320 0.687 0.297 0.659 0.765 0.380 0.622	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 53.31 0.627 3599 0.128 1.5 0.540 1.44 0.550 1.44 0.550 1.44 0.550 1.44 0.550 1.44 0.550 1.3 0.564 1.8 0.056 0.8 0.561 6.8 0.056 6.8 0.018 4.68 0.018 4.68 0.048 2.9 0.115 74.00 0.048 0.29 0.115 74.00 0.049 0.20	660         -0.78           223         -1.33           024         -1.75           029         3.11           991         0.51           554         1.52           911         0.51           554         1.52           912         0.61           914         0.51           915         1.62           916         0.44           917         0.51           928         -0.10           929         1.50           922         -0.10           929         1.50           920         0.52           921         0.52           922         -0.10           924         0.52           930         0.52           931         0.52           932         -0.10           942         0.52           933         0.54           943         -0.72           943         -0.72           943         -0.72           944         -0.70           945         -0.70	19         0.430           15         0.181           16         0.000           17         0.161           10         0.611           10         0.611           10         0.611           10         0.133           12         0.191           10         0.254           10         0.254           12         0.911           13         0.257           13         0.251           13         0.351           13         0.351           13         0.451           13         0.451           14         0.451           15         0.454           16         0.451           17         0.151           13         0.454           14         0.481	0 2 2 0 3 8 8 2 2 9 9 2 0 8 8 2 2 7 7 9 2 0 8 8 2 2 7 7 8 8 8 4 4 8 8 1 7 7 8 8 2 2 5 7 7 9 8 8 2 2 9 9 7 7 7 9 9 8 8 8 9 2 9 9 9 9 9 9 9 9 9 9 9 9 9	
	Al Tmimi, 2016 Humphreys, 2016 Kazmienski, 2014s Khan, 2014 Li, 2015 Loporen, 2008 Mardani, 2012 Martin, 2010 Matin, 2010 Mikelic, 2012 Norkeine, 2007 Oldham, 2015 Oldham, 2015 Ringsidene, 2015 Rudolph, 2009 Rudolph, 2006 Santana Santos, 2004 Sewk, 2015 Taganakis, 2007 Tully, 2010	0.595 0.505 0.436 1.978 2.273 4.727 0.441 0.900 1.095 1.123 0.970 1.955 0.275 1.851 1.320 0.667 2.913 0.297 0.659 0.725 0.639 0.725 0.639 0.622 1.480	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 5330 0.627 3539 0.627 3539 0.627 3539 0.627 1.28 1.5 0.564 1.48 0.937 1.22 0.905 1.3 0.564 1.48 0.656 1.3 0.564 1.48 0.656 0.83 0.561 6.8 0.561 1.2 0.561 1.2	660         -0.78           223         -1.33           024         -1.75           029         3.111           991         0.51           554         1.52           911         0.51           912         -1.25           914         0.51           915         -1.25           916         0.44           917         0.41           918         -1.25           917         0.44           918         -1.25           917         0.444           926         -0.07           828         -0.52           910         0.444           927         0.68           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           93         0.52           94         -0.77           1.44         0.26           95         1.26           95         1.26           96         0.77           97         1.444     <	19         0.430           15         0.181           16         0.000           17         0.161           10         0.131           12         0.191           12         0.191           13         0.225           14         0.000           15         0.133           16         0.133           17         0.151           13         0.251           13         0.251           13         0.251           13         0.251           13         0.451           13         0.451           14         0.433           15         0.132           16         0.132           17         0.151           13         0.451           14         0.431           14         0.431           14         0.431           14         0.431	0 2 2 0 3 8 2 2 9 9 2 0 5 5 2 7 7 9 2 0 5 5 2 2 7 7 8 8 5 4 4 5 5 2 2 7 7 9 2 2 0 2 2 0 3 8 2 2 2 0 5 2 2 0 5 2 2 0 5 5 5 5 5 5 5 5	
	Al Tmimi, 2016 Humphreys, 2016 Kaznierski, 2014 Khar, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscafor, 2012 Martin, 2010 Miskiic, 2012 Norkeine, 2017 Oldham, 2013 Palmbargan, 2012 Ringalitere, 2015 Rudolph, 2009 Rudolph, 2009 Santana Santos, 2004 Servak, 2015 Tagarakis, 2007 Tully, 2016 Zhang, 2016	0.595 0.500 0.436 1.378 2.273 4.727 0.441 0.900 1.975 1.320 0.970 1.975 1.321 0.975 1.351 1.322 0.667 2.913 1.322 0.667 0.275 0.389 0.275 0.389 0.275 0.389 0.275 0.389 0.237 0.459 0.230 0.230 0.230 0.231 0.421 0.421 0.421 0.421 0.421 0.421 0.421 0.421 0.425 0.235 0.	0.164 2.10 0.229 1.3 0.172 1.11 1.286 3.00 0.097 5330 0.627 5530 0.627 5595 0.128 1.5 0.626 1.4 0.937 1.2 0.936 1.3 0.564 1.8 0.564 1.8 0.656 1.8 0.078 2.4 0.155 4.8 0.078 1.4 0.078 1.4 0.078 1.4 0.078 1.4 0.078 1.4 0.037 1.4 0.078 1.4	660         -0.78           223         -1.33           024         -1.75           029         3.11           1991         0.51           54         1.52           911         0.51           54         1.52           911         0.41           955         1.62           920         -0.70           822         -0.10           826         -1.22           911         0.414           922         -0.10           826         -0.70           827         0.89           833         0.64           842         -0.77           1.41         -0.32           173         -1.41           174         -0.22           173         -1.41           174         -0.22           175         1.25           177         -0.42           928         -0.78           174         -0.22           175         -1.25           177         -1.41           174         -0.22           175         -1.25           185	19         0.4304           15         0.1815           15         0.1816           16         0.000           10         0.616           10         0.616           10         0.616           10         0.616           10         0.616           10         0.616           10         0.625           13         0.252           14         0.000           13         0.252           14         0.0001           15         0.517           16         0.0001           12         0.799           13         0.264           13         0.476           14         0.477           15         0.372           14         0.479           14         0.479           19         0.332           19         0.332           19         0.332           10         0.256	0 2 2 0 3 3 8 2 2 7 7 8 8 2 2 7 7 8 8 8 1 2 2 0 5 8 2 7 7 7 8 8 2 2 0 5 8 2 2 0 5 2 0 5 2 0 5 2 0 5 2 0 5 2 0 5 2 0 5 5 5 5	

Kidney injury	Study name		Statist	ics for ea	ach study	L	Odds ratio and 95% CI
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
	Leenders, 2018	4.744			4.104	0.000	
	Humphreys, 2016	1.010			0.015		
	Mardani, 2012	1.973				0.127	
	Martin, 2010	1.918					
	Martin, 2012	1.607					
	Mu, 2010	1.229				0.763	
	Nikolic, 2012	1.045				0.913	
	Omiya, 2015	4.000	0.217	73.618	0.933	0.351	
	Otomo, 2013	1.814	0.361	9.126	0.723	0.470	
	Ringaitiene, 2015	2.106	0.093	47.538	0.468	0.640	
	Santana Santos, 2004	5.547	1.677	18.352	2.806	0.005	
	Tully, 2010	0.473	0.098	2.275	-0.935	0.350	
	Zhang, 2015	2.492	1.030	6.032	2.025	0.043	<del>     </del>
	Oh, 2017	3.060	1.120	8.360	2.181	0.029	
		1.944	1.502	2.517	5.044	0.000	♦
							0.1 0.2 0.5 1 2 5 10
Previous MI <30 days	Study name	S	Statistic	s for ea	ch stud	y	Odds ratio and 95% CI
	0	dds L	ower l	Jpper			
	ra	atio	limit	limit	Z-Value	p-Value	
	Humphreys, 2016 0	.940	0.476	1.855	-0.178	0.858	
	and the second sec		0.498	6.687	0.907	0.364	
			1.552		2.820	0.005	
				7.547		0.502	
	Ringaitiene, 2015 1				0.672		
	State of		0.574	2.394	0.435	0.663	
	1	.543	0.898	2.653	1.570	0.116	🔶
							0.1 0.2 0.5 1 2 5 10
Previous MI history/ever	Study name		Statist	ice for o	ach study		Odds ratio and 95% Cl
	<u>Study name</u>	Odds	Lower	Upper		-	
		ratio	limit	limit	Z-Value	p-Value	
	Caldas, 2019	1.024			0.033	0.974	
	Chen, 2017	2.037			1.852	0.064	
	Dong, 2014	1.478	0.669		0.966	0.334	
	Eriksson, 2002	1.222		4.448	0.304	0.761	
	Gottesman, 2010	1.241				0.076	
	Coffey, 1983	1.135				0.716	
	Mariscalco, 2012	1.056				0.801	🖊 🕂
	Omiya, 2015	2.933		22.463		0.300	
	Ringaitiene, 2015	0.784				0.742	
	Santana Santos, 2004	0.675				0.183	│ │ ┼╾┼ │ │ │
	Yilmaz, 2016	0.860				0.851	
		1.169	0.984	1.388	1.779	0.075	
							0.1 0.2 0.5 1 2 5 1

revious stroke, TIA, CVA	Study name		Statisti	cs for ea	ch study		Odds ratio and 95% Cl
		Odds I ratio	Lower limit	Upper limit	Z-Value	p-Value	
	Caldas, 2019	0.719	0.075	6.915	-0.286	0.775	
	Chen, 2017	0.914	0.363	2.300	-0.192	0.848	
	Leenders, 2018	1.765	0.760	4.100	1.321	0.186	
	Dong, 2014	2.603	0.714	9.490	1.449	0.147	
	Eriksson, 2002	9.486	1.475	60.991	2.370	0.018	
	Gottesman, 2010	2.309	1.683	3.168	5.190	0.000	
	Khan, 2014	18.365	2.130	158.346	2.648	0.008	
	Mardani, 2012	2.709	1.102	6.662	2.171	0.030	
	Mariscalco, 2012	2.545	1.389	4.666	3.022	0.003	<b> - ∎</b> -
	Martin, 2010	3.895	2.869	5.290	8.709	0.000	
	Miyazaki, 2011	2.150	1.365	3.386	3.304	0.001	
	Mu, 2010	1.924	0.879	4.212	1.637	0.102	++++-
	Norkeine, 2007	1.400	0.422	4.644	0.550	0.582	│ │ <del>│ ┼┱╡</del> ──│ │
	Palmbergen, 2012	7.781	2.063	29.354	3.029	0.002	
	Rolfson, 1999a	6.769	1.178	38.898	2.144	0.032	
		2.546	1.936	3.350	6.680	0.000	
							0.1 0.2 0.5 1 2 5 10
VD	Study name		Statieti	ice for ea	ich study	ė	Odds ratio and 95% Cl
	Study hame	Odda	Lower	Upper	ich study		
		Odds ratio	limit	limit	Z-Value	p-Value	
	Caldas, 2019	0.458	0.051	4.107	-0.697	0.486	k → ∎ → ↓ → ↓
	Leenders, 2018	1.982	0.881	4.459	1.653		
	Coffey, 1983	0.982	0.232	4.160	-0.025		
	Humphreys, 2016	1.130	0.417	3.065	0.240		
	Kazmierski, 2014a	2.295	0.905	5.816	1.751	0.080	
	Kazmierski, 2014b	1.871	0.616	5.683	1.105	0.269	
	Mariscalco, 2012	1.498	0.910		1.589	0.112	
	Martin, 2012	2.159	1.765	2.642	7.478	0.000	
		10.733	3.963		4.669	0.000	
	Norkeine, 2007	2.790	1.303	5.970	2.643	0.008	
	Otomo, 2013	3.314	1.088		2.109	0.035	
	Ringaitiene, 2015	2.130	0.468		0.978		
	Sevuk, 2015	0.854	0.253	2.881	-0.254	0.799	
	Tully, 2010	1.128	0.397	3.203	0.226	0.821	
	ruiy, 2010	1.977	1.482		4.636	0.000	
		1.511	1.402	2.001	4.000	0.000	0.1 0.2 0.5 1 2 5 1
	-						
moking current	Study name				each stud	ły	Odds ratio and 95% Cl
		Odds ratio		Upper limit		p-Value	
	Caldas, 2019	0.343	3 0.06	9 1.697	7 - <mark>1.31</mark> 2	0.190	<del>K <b>I ■ I</b> −</del> I I
	Chen, 2017	0.442	2 0.21			0.029	
			1	9 2.113	-0.066	0.948	
	Dong, 2014	0.974					
	Dong, 2014 Kazmierski, 2014b	0.46	7 0.15	5 1.405	5 - <mark>1.3</mark> 55		│ ┼─╋╶┼╴│_ │
	Dong, 2014 Kazmierski, 2014b Khan, 2014	0.467 2.886	7 0.15 6 2.01	5 1.405 6 4.132	5 -1.355 2 <mark>5.78</mark> 9	0.000	│ <del>┼</del> ╇ <del>┦</del> ┝ <u></u> ╸│
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012	0.467 2.886 8.358	7 0.15 6 2.01 8 1.85	5 1.405 6 4.132 0 37.764	5 -1.355 2 5.789 4 2.759	<ul><li>0.000</li><li>0.006</li></ul>	│ <del>│ <b>●</b> <del>┃</del> </del>
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010	0.467 2.886 8.356 1.147	7 0.15 6 2.01 8 1.85 7 0.97	5 1.405 6 4.132 0 37.764 1 1.354	5 -1.355 2 5.789 4 2.759 4 1.611	<ul> <li>0.000</li> <li>0.006</li> <li>0.107</li> </ul>	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007	0.46 2.886 8.358 1.14 1.053	7         0.15           6         2.01           8         1.85           7         0.97           3         0.43	5 1.405 6 4.132 0 37.764 1 1.354 8 2.536	5 -1.355 2 5.789 4 2.759 4 1.611 5 0.116	<ul> <li>0.000</li> <li>0.006</li> <li>0.107</li> <li>0.908</li> </ul>	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015	0.46 2.880 8.358 1.14 1.053 1.600	7         0.15           6         2.01           8         1.85           7         0.97           3         0.43           0         0.23	5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809	5 -1.355 2 5.789 4 2.759 4 1.611 5 0.116 9 0.482	0.000           0.006           0.107           0.908           0.630	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013	0.465 2.886 8.358 1.145 1.055 1.600 2.012	7         0.15           6         2.01           8         1.85           7         0.97           3         0.43           0         0.23           2         0.61	5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809 7 6.562	5 -1.355 2 5.789 4 2.759 4 1.611 6 0.116 9 0.482 2 1.159	0.000         0.000           0.006         0.107           0.908         0.908           0.630         0.246	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005	0.467 2.880 8.350 1.147 1.053 1.600 2.012 1.545	7         0.153           6         2.010           8         1.850           7         0.97           3         0.433           0         0.233           2         0.611           5         0.313	5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809 7 6.562 8 7.502	5 -1.355 2 5.789 4 2.759 4 1.611 5 0.116 9 0.482 2 1.159 2 0.540	0.000           0.006           0.107           0.908           0.630           0.246           0.589	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004	0.467 2.880 8.356 1.147 1.055 1.600 2.012 1.545 1.962	7         0.153           6         2.010           8         1.850           7         0.97           3         0.433           0         0.233           2         0.611           5         0.313           2         0.933	5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809 7 6.562 8 7.502 5 4.118	5 -1.355 2 5.789 4 2.759 4 1.611 6 0.116 9 0.482 2 1.159 2 0.540 3 1.781	0         0.000           0         0.006           1         0.107           5         0.908           2         0.630           0         0.246           0         0.589           1         0.075	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004 Sevuk, 2015	0.46 2.886 8.356 1.14 1.055 1.600 2.012 1.545 1.962 0.748	7         0.153           6         2.010           8         1.850           7         0.97           3         0.433           0         0.233           2         0.611           5         0.313           2         0.933           8         0.413	5         1.405           6         4.132           0         37.764           1         1.354           8         2.536           7         10.809           7         6.562           8         7.502           5         4.118           3         1.356	5         -1.355           2         5.789           4         2.759           4         1.611           6         0.116           9         0.482           2         1.159           2         0.540           3         1.781           6         -0.958	9         0.000           9         0.006           1         0.107           6         0.908           2         0.630           9         0.246           0         0.589           1         0.075           3         0.338	
	Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004	0.467 2.886 8.356 1.147 1.055 1.600 2.012 1.545 1.962	7         0.15           6         2.01           8         1.85           7         0.97           3         0.43           0         0.23           2         0.61           5         0.31           2         0.93           8         0.41           5         0.64	5       1.405         6       4.132         0       37.764         1       1.354         8       2.536         7       10.809         7       6.562         8       7.502         5       4.118         3       1.356         9       1.918	5         -1.355           2         5.789           4         2.759           4         1.611           6         0.116           9         0.482           2         1.159           2         0.540           3         1.781           6         -0.958           3         0.395	9         0.000           9         0.006           1         0.107           6         0.908           2         0.630           9         0.246           0         0.589           1         0.075           3         0.338           5         0.693	

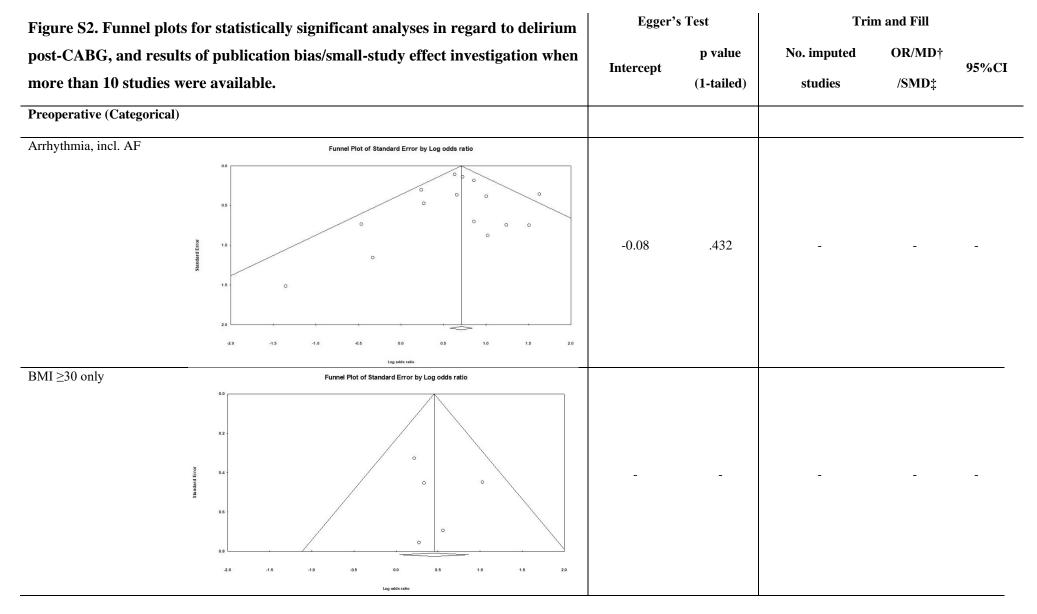
Smoking current/history	Study name		Statisti	cs for ea	ach study	!		Odds ra	atio and 95%	CI
		Odds ratio	Lower limit		Z-Value	p-Value				
	Caldas, 2019	0.644		2.093	-0.732	0.464				
	Chen, 2017	0.442		0.921	-2.179	0.029				
	Oldham, 2018	1.492		3.987	0.798			-	-	
	Dong, 2014	0.974	0.449	2.113	-0.066	0.948		- I - I-	-	
	Gottesman, 2010	1.145	0.893	1.468	1.065	0.287				
	Coffey, 1983	0.974		2.105	-0.066	0.948			-	
	Humphreys, 2016	1.110	0.561	2.195	0.300					
	Kazmierski, 2014b	0.467	0.155	1.405	-1.355	0.175				
	Khan, 2014 Mardani, 2012	2.886	2.016	4.132 37.764	5.789 2.759				28	
	Martin, 2012	1.147	0.971	1.354	1.611	0.107	<u>}</u>			-
	Miyazaki, 2011	1.323	0.848	2.065	1.232					
	Mu, 2010	0.929	0.543	1.589	-0.271	0.787				
	Norkeine, 2007	1.053	0.438	2.536	0.116		5	2	-	4
	O miy a, 2015	1.600	0.237	10.809	0.482	0.630	8	3 <u></u>	-	
	Otomo, 2013	2.012	0.617	6.562	1.159	0.246			+ +	
	Ringaitiene, 2015	1.263	0.236	6.766	0.273					-
	Rudolph, 2005	1.545	0.318	7.502	0.540	0.589		1. Contraction of the second sec		-
	Santana Santos, 200		0.604	1.858	0.201	0.841				
	Sevuk, 2015	0.748	0.413	1.356	-0.958	0.338				
	Zhang, 2015	1.115		1.918	0.395					
		1.153	0.939	1.415	1.360	0.174	0.1	0.2 0.5	1 2	5 1
Pre-Operative (Continuous)										
• ` ` `										
Age (years) *	Study name		100	s for each	0.000			Difference	ce in means and 9	5% CI
	Differe in me			Lower ice limit		Z-Value p-V	alue			
	Caldas, 2019 5	.000 2	625 6.8	93 -0.14	6 10.146	1.904 0	.057	1 1		• *
			423 2.0 438 2.0				.232		-	-
				17 -0.15			059			
			531 12.4 399 1.9				178		-	• •
			834 3.3				.022			
			177 4.7 442 2.0	39 -1.51 79 3.84			.207			
	100000000000000000000000000000000000000		862 0.7				049		<b></b>	1000
		.000 3.								
				62 5.26			.001			
	Loponen, 2008 6	.200 2.	163 4.6 233 4.9	79 1.96	0 10.440	2.866 (		-	• -	
	Loponen, 2008 6 Mardani, 2012 -2 Mariscalco, 2012 5	200 2 070 2 000 0	163 4.6 233 4.9 997 0.9	79 1.96 85 -6.44 95 3.04	0 10.440 6 2.306 5 6.955	2.800 0 -0.927 0 5.013 0	001 004 354 000	-	•+	<b>.</b>
	Loponen, 2008 6 Mardani, 2012 -2 Mariacalco, 2012 5 Mu, 2010 5	200 2 .070 2 .000 0 .300 1	163 4.6 233 4.9	179 1.96 185 -6.44 195 3.04 114 3.32	0 10.440 6 2.306 5 6.955 8 7.274	2.866 ( -0.927 ( 5.013 ( 5.262 (	.001 .004 .354		•	
	Loponen, 2008 6 Mardani, 2012 -2 Marizato, 2012 5 Mu, 2010 8 Norkeine, 2007 8 Oldham, 2015 55	200 2. 070 2. 000 0. 300 1. 800 1. 800 2.	163 4.6 233 4.9 997 0.9 007 1.0 434 2.0 543 6.4	79 1.98 85 -6.44 95 3.04 14 3.32 56 2.99 85 0.81	0 10.440 6 2.306 5 6.955 8 7.274 0 8.610 7 10.583	2.888 ( -0.927 ( 5.013 ( 6.282 ( 4.045 ( 2.202 (	001 004 354 000 000 000 028			
	Loponen, 2008 8 Mardani, 2012 -2-2 Mariaselo, 2012 5 Mu, 2010 8 Norkeine, 2007 8 Oldham, 2015 5 Otomo, 2013 1	200 2. 070 2. 000 0. 300 1. 800 1. 800 2. 000 1.	163 4.6 233 4.9 997 0.9 007 1.0 434 2.0	79 1.98 (85 -6.44) (95 3.04) (14 3.32) (56 2.99 (85 0.61) (95 -2.55)	0 10.440 6 2.306 5 6.955 6 7.274 0 8.610 7 10.583 8 4.558	2.886 ( 0.927 ( 5.013 ( 5.262 ( 4.045 ( 2.202 ( 0.551 (	.001 .004 .354 .000 .000			
	Loponen, 2008 6 Mardani, 2012 -2 Mariasalco, 2012 5 Mu, 2010 5 Norkeine, 2007 5 Oldham, 2015 5 Otomo, 2013 7 Palmbergen, 2012 7 Plaschie, 2010 6	200 2. 070 2. 000 0. 300 1. 800 1. 520 1. 000 1.	163         4.6           233         4.9           997         0.9           007         1.0           434         2.0           543         6.4           815         3.2           318         1.7           775         3.1	179         1.96           185         -6.44           195         3.04           194         3.32           195         2.99           165         0.61           195         -2.55           136         4.93           150         2.52	0 10.440 6 2.308 5 6.955 6 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479	2.886 ( 0.927 ( 5.013 ( 5.262 ( 4.045 ( 2.202 ( 0.551 ( 5.707 ( 3.380 (	001 004 354 000 000 000 028 582 000 001			
	Loponen, 2008 6 Mardani, 2012 -2-2 Mariaxaiso, 2012 5 Mu, 2010 8 Norkeine, 2007 5 Oldham, 2015 5 Otomo, 2013 1 Palmbergen, 2012 7 Plaschie, 2010 6 Ringaitene, 2015 2	200         2           .070         2           .000         0           .300         1           .800         1           .800         1           .520         1           .000         1           .520         1           .500         2	163 4.6 233 4.9 997 0.9 007 1.0 434 2.0 543 6.4 815 3.2 318 1.7	179         1.96           185         -6.44           195         3.04           114         3.32           156         2.99           165         0.61           195         -2.55           136         4.93           150         2.52           154         -3.13	0 10.440 6 2.306 5 6.955 6 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479 4 8.134	2.886 ( 0.927 ( 5.013 ( 5.202 ( 4.045 ( 2.202 ( 0.551 ( 5.707 ( 3.380 ( 0.870 (	001 004 354 000 000 000 028 582 000			
	Loponen, 2008 6 Mardani, 2012 -2 Mariabalco, 2012 5 Mu, 2010 5 Oldham, 2015 5 Otomo, 2013 1 Palmbergen, 2012 7 Plaschie, 2010 6 Ringalitene, 2015 8 Rudolph, 2009 8 Rudolph, 2006 2	200         2.           .070         2.           .000         0.           .300         1.           .800         1.           .600         2.           .000         1.           .520         1.           .500         2.           .600         1.           .500         2.           .800         1.           .500         2.           .800         1.	163         4.6           233         4.9           997         0.8           007         1.0           434         2.0           543         6.4           816         3.2           318         1.7           775         3.1           876         8.2           365         1.8	179         1.96           185         -6.44           195         3.04           114         3.32           156         2.99           165         0.61           136         2.99           136         4.93           156         2.52           164         -3.13           142         5.23	0 10.440 6 2.306 5 6.955 8 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479 4 8.134 8 11.962 5 4.875	2.886 ( 0.927 ( 5.013 ( 5.262 ( 4.045 ( 2.202 ( 0.5707 ( 3.380 ( 0.870 ( 5.014 ( 1.612 (	001 004 354 000 000 028 582 000 001 384 000 107			
	Loponen, 2008 6 Mardani, 2012 -2- Mariasico, 2012 -2- Mariasico, 2012 -5 Olomo, 2013 5 Olomo, 2013 1 Palmbergen, 2012 7 Plaschie, 2010 7 Ringalicene, 2015 2 Rudolph, 2009 8 Rudolph, 2009 8 Rudolph, 2009 2 Santana Santoa, 2004 2 Sevuk, 2015 -1	200         2.           070         2.           0800         0.           300         1.           800         2.           000         1.           520         1.           500         2.           800         1.           500         2.           800         1.           500         2.           800         1.           200         1.           200         1.           200         0.           100         0.	163         4.6           233         4.5           997         0.5           007         1.0           434         2.0           543         6.4           816         3.2           318         1.7           775         3.1           876         8.2           715         2.5           365         1.6           586         0.3	179         1.96           185         -6.44           195         3.04           114         3.32           156         2.99           195         -2.55           136         4.93           150         2.52           154         -3.13           142         5.23           153         -0.47           116         1.34           143         -2.243	0 10.440 6 2.308 5 0.955 6 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479 4 8.134 8 11.962 5 4.875 2 4.418 9 0.049	2.886 ( 0.927 ( 5.013 ( 5.262 ( 4.045 ( 2.202 ( 0.551 ( 5.707 ( 3.380 ( 0.870 ( 5.014 ( 1.612 ( 3.669 ( 4.877 (	001 004 354 000 000 028 582 000 001 384 000 107 000 107 000			
	Loponen, 2008 6 Mardani, 2012 -2 Mariabalco, 2012 5 May 2010 6 Norkeine, 2007 5 Oldham, 2015 5 Otomo, 2013 1 Palmbergen, 2012 7 Plaschke, 2010 6 Ringaitiane, 2015 2 Rudolph, 2008 8 Rudolph, 2008 2 Santana Santos, 2004 2 Savuk, 2015 -1 Siepe, 2011 6	200         2.           070         2.           000         0.           300         1.           800         2.           000         1.           500         2.           000         1.           500         2.           800         1.           500         2.           800         1.           500         2.           800         1.           200         1.           880         0.           100         0.           200         3.	163         4.6           233         4.9           997         0.5           007         1.0           434         2.0           543         6.4           816         3.2           318         1.7           775         3.1           875         8.2           716         2.9           365         1.8           785         0.3           816         14.5	179         1.980           185         -6.444           195         3.044           196         3.044           196         3.044           196         2.99           185         0.61           195         2.564           136         4.93           150         2.52           184         -3.13           183         -0.471           161         1.344           43         -2.244	0 10.440 8 2.308 5 8.955 8 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479 4 8.134 8 11.962 5 4.875 2 4.418 9 0.049 0 13.680	2.886 ( 0.927 ( 5.013 ( 6.262 ( 0.551 ( 0.551 ( 0.551 ( 0.870 ( 0.870 ( 0.870 ( 0.870 ( 0.870 ( 0.870 ( 0.877 ( 1.612 ( 0.877 ( 1.625 ( 0.877	001 004 354 000 000 000 000 582 582 000 001 384 000 107 107 000 0061 104			
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BMI	Loponen, 2008 6 Mardani, 2012 -2 Marixaalo, 2012 5 Mu, 2010 8 Norkeine, 2007 5 Oldham, 2015 5 Oldham, 2015 1 Palmbergen, 2012 7 Plaschke, 2010 6 Ringalisene, 2015 2 Rudolph, 2006 8 Rudolph, 2006 8 Rudolph, 2006 2 Santana Santoa, 2004 2 Sevuk, 2015 -1 Siepe, 2011 6 Tully, 2010 2 Zhang, 2015 2	200 2. .070 2. .070 2. .000 0. .800 1. .800 1. .800 1. .520 1. .500 2. .600 1. .520 1. .500 2. .600 1. .520 1. .500 2. .600 1. .520	183         4.6.           223         4.9.           997         0.8.           0007         1.0.           434         2.0.           543         6.4.           815         3.2.           318         1.7.           875         8.2.           715         3.8.           785         0.0.           886         0.3.           816         14.6.           819         3.2.           227         1.6.           610         0.3.	179         1.90           185         6.44           114         3.32           156         2.99           186         6.11           195         -2.55           136         4.93           150         2.52           154         -3.13           142         5.23           153         -4.41           136         -2.24           161         1.34           143         -2.24           163         -1.28           163         -1.28           172         2.94           s for each         s	0 10.440 5 2.306 5 0.955 5 7.274 0 8.610 7 10.583 8 4.556 7 10.103 1 9.479 4 8.134 8 11.34 8 11.34 8 11.34 8 1.134 8 1.134 9 0.049 0 13.680 1 3.680 1 3.639 8 5.339 study	2.886 ( 0.927 ( 5.013 ( 5.022 ( 4.046 ( 2.202 ( 0.551 ( 5.070 ( 3.380 ( 0.870 ( 3.380 ( 0.870 ( 1.612 ( 3.669 ( 1.612 ( 1.6	001 004 354 000 000 000 0028 582 000 001 384 000 107 000 107 000 001 107 000 001		e	
BMI	Loponen, 2008 6 Mardani, 2012 -2- Marianaico, 2012 -2- Mu, 2010 8 Norkeine, 2007 5 Oldham, 2015 5 Oldham, 2015 1 Palmbergen, 2012 7 Plaschie, 2010 7 Plaschie, 2010 8 Rudolph, 2008 8 Rudolph, 2009 8	200 2. .070 2. .070 2. .070 0. .000 0. .000 1. .800	183         4.6           233         4.9           997         0.8           0007         1.0           434         2.0           543         6.4           815         3.2           715         3.1           875         2.2           715         3.8           816         1.4           819         3.3           287         1.0           610         0.3	179         1.90           185         6.44           14         3.02           14         3.32           156         2.99           165         2.51           195         -2.56           136         -9.31           150         2.52           163         -0.471           164         -1.31           163         -2.471           163         -2.241           163         -1.281           0.7         -1.061           157         0.082           172         2.941           s for each         Lower           text         Imit	0 10.440 6 2.306 5 0.955 6 7.274 0 8.610 7 10.583 8 4.558 8 4.558 8 4.558 8 4.558 8 4.558 9 0.049 0 13.680 4 6.084 7 5.133 8 5.339 study Upper limit	2.866 ( 0.927 ( 5.013 ( 5.043 ( 2.202 ( 0.551 ( 2.202 ( 0.551 ( 5.707 ( 5.707 ( 5.014 ( 0.551 ( 5.707 ( 5.014 ( 0.551 ( 5.707 ( 5.014 ( 5.019 ( 5.019) ( 5.019 ( 5.019) ( 5.019) ( 5.019) (	001 004 054 000 000 000 000 000 000 000 000			
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BMI	Loponen, 2008 0 Mardani, 2012 -2- Mariauaico, 2012 -2- Mu, 2010 5 Norkeine, 2010 5 Oldham, 2015 5 Olomo, 2013 1 Palmbergen, 2012 7 Plasofike, 2010 6 Ringaitiene, 2015 2 Rudolph, 2009 8 Rudolph, 2009 8 Rudolph, 2009 8 Santana Santoa, 2004 2 Sevuk, 2015 -1 Siepe, 2011 6 Tully, 2010 2 Zhang, 2015 2 Multiple Santoa Difference in means Leenders, 2018 -0.77 Dong, 2014 0.77	200 2. .070 2. .070 2. .000 0. .000 0. .000 1. .500 1. .520 1. .500 1. .520 1. .500 1. .520 1. .500 1. .500 2. .600 1. .500	183         4.6           223         4.5           223         4.5           97         0.5           97         0.5           97         1.0           434         2.0           543         6.4           815         3.2           318         1.7           715         2.5           365         1.8           755         0.3           816         1.45           819         3.2           287         1.6           610         0.3           Variance           37         0.44           84         0.22	199         1.90           195         1.90           195         3.044           114         3.321           114         3.321           114         3.321           1155         2.523           126         2.93           1365         2.523           136         -0.471           138         -0.471           139         -2.553           130         -0.471           130         -0.471           130         -0.471           131         -0.483           132         -0.443           133         -0.471           143         -2.244           157         0.082           172         2.944           12         1.94           12         1.94           12         1.94           134         -0.244	0 10.440 5 2.306 5 0.955 8 7.274 0 8.610 7 10.583 8 4.558 7 10.103 1 9.479 4 8.134 8 1.190 5 4.875 2 4.418 9 0.049 0 13.680 4 0.049 0 13.680 4 8.5339 <b>study</b> <b>study</b> <b>study</b> 9 1.649	2.886 ( 0.927 ( 5.013 ( 5.282 ( 4.045 ( 2.202 ( 0.551 ( 0.551 ( 0.551 ( 0.870 ( 3.380 ( 0.870 ( 3.380 ( 0.877 ( 1.812 ( 1.817 ( 1.825 ( 1.877 ( 1.825 ( 0.877 ( 1.825 ( 1.825 ( 0.877 ( 1.825	.001 .004 .004 .000 .000 .000 .000 .000			
BMI	Loponen, 2008 6 Mardani, 2012 -2- Mariasaico, 2012 5 Mu, 2010 8 Norkeine, 2007 5 Oldham, 2015 1 Palmbergen, 2012 7 Plaschie, 2010 7 Plaschie, 2010 8 Rudolph, 2009 8 Rudolph, 2005 2 Santana Santos, 2004 2 Santana Santos, 2004 2 Santana Santos, 2004 2 Study name Difference in means Leenders, 2018 -0.7/	200 2. .070 2. .070 2. .000 0. .000 0. .300 1. .800 1. .800 1. .520 1. .500 1. .520 1. .520 1. .520 1. .540	183         4.6           233         4.9           233         4.9           234         4.9           97         0.9           007         1.0           434         2.0           543         6.4           816         3.2           318         1.7           715         2.5           365         1.8           816         4.6           817         3.2           365         1.8           810         0.3           0         Variance           37         0.44           84         0.23           46         0.11	179         1.90           185         6.44           185         6.44           114         3.21           114         3.22           116         0.11           115         2.52           116         1.34           1195         -2.55           110         5.23           110         3.0.47           111         1.34           112         2.24           116         1.34           116         1.34           117         2.94           117         2.94           117         2.94           117         1.94           117         2.94           117         1.94           117         2.94	0         10.440           6         2.306           5         6.955           5         7.274           0         8.610           7         10.583           7         10.583           8         4.558           7         10.103           9         4.79           4         8.134           6         1.482           5         4.875           2         4.418           9         0.049           0         13.680           8         5.339           study           Upper Upmer           8         0.548           9         1.649           4         0.674	2.866 ( 0.927 ( 5.013 ( 2.002 ( 4.045 ( 2.202 ( 0.551 ( 5.707 ( 3.380 ( 0.551 ( 5.707 ( 3.380 ( 0.570 ( 5.014 ( 1.612 ( 3.689 ( -1.877 ( 2.028 ( 6.792 ( -1.100 ( -1.100 ( -0.51 ( -0.51 ( 0.51	001 004 004 006 000 000 000 000 000			
BMI	Loponen, 2008 0 Mardani, 2012 -2- Mariaxalico, 2012 -2- Mu, 2010 5 Norkeine, 2010 5 Oldham, 2015 5 Oldham, 2015 5 Oldham, 2015 2 Rudolph, 2009 8 Rudolph, 2009 8 Rudolph, 2009 8 Santana Santoa, 2004 2 Santana Sa	200 2. .070 2. .070 2. .070 2. .070 1. .070 0. .070	183         4.6           223         4.9           223         4.9           97         0.9           007         1.0           434         2.0           543         6.4           815         3.2           318         1.7           715         2.1           875         0.6           586         0.3           287         1.6           810         0.3            37           04         0.22           46         0.11           05         0.25	179         1.90           185         6.44           185         6.44           185         6.44           185         3.04           186         2.99           186         2.99           186         2.91           195         -2.55           136         4.93           150         2.52           183         -0.47           116         1.34           142         5.23           183         -0.47           103         -1.28           103         -1.24           103         -1.28           103         -1.28           104         -1.08           157         0.08           172         2.94           107         -1.08           107         -1.94           34         -0.24           34         -0.24           34         -0.24           35         -0.98	0         10.440           6         2.306           5         9.955           8         7.274           0         8.610           7         10.583           8         4.558           7         10.103           9         479           4         8.134           5         4.875           2         4.418           9         0.049           0         13.680           13.880         5.339           study           Light colspan="2">study           8         5.339           study           study           8         0.548           9         1.649           4         0.674           0         1.000	2.886 ( 0.927 ( 5.013 ( 5.262 ( 4.045 ( 0.551 ( 0.551 ( 0.551 ( 0.551 ( 0.551 ( 0.551 ( 0.551 ( 0.577 ( 1.317 ( 1.612 ( 1.375 ( 2.028 ( 6.792 ( 0.792 ( 0.792 ( 0.792 ( 0.792 ( 0.100 ( 1.446 ( 0.100 ( 0.100)	.001 .004 .004 .000 .000 .000 .000 .000			
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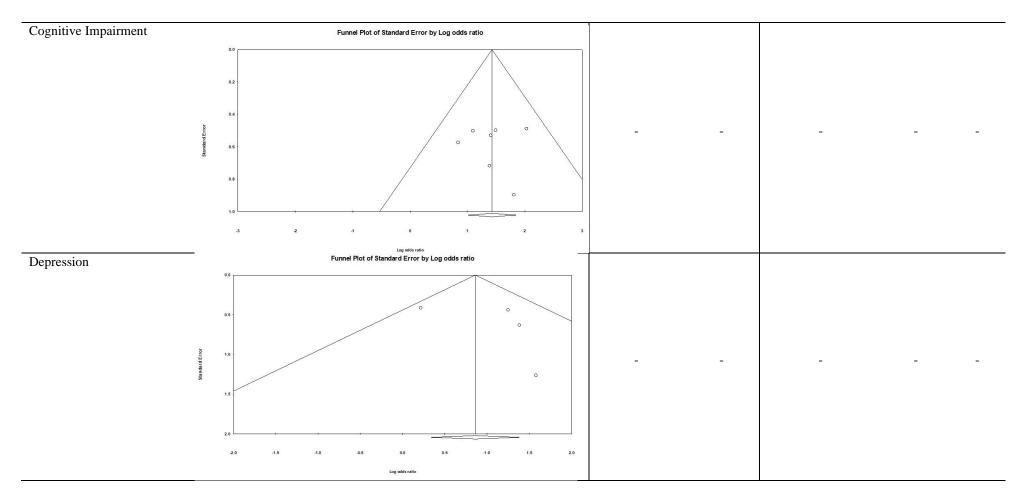
Cognition: All tests	Study name		S	tatistics for	r each st	tudy				Std diff	in means and	95% CI	
	18		Standard	1	Lower	Upper							
		in means	error	Variance	limit	limit 2	Z-Value p	-Value					
	Caldas, 2019	-1.059	0.295	0.087	-1.638	-0.481	-3.588	0.000	-				
	Chen, 2017	-0.316	0.184	0.034	-0.677	0.046	-1.712	0.087					
	Oldham, 2018	-0.445	0.240	0.057	-0.914	0.025	+1.855	0.064			1		
	Al Tmimi, 2016 Kazmierski, 2014a	0.000	0.258	0.066	-0.505	0.505	0.000 -3.654	1.000					
	Li, 2015	-0.912	0.464	0.215	-1.821	-0.004	-1.968	0.049	22		8		
	Oldham, 2015	-0.784	0.293	0.086	-1.359	-0.210	-2.678	0.007	32 <u>8</u>	6 - 19 <u>16</u> - 1	18		
	Otomo, 2013	-0.772	0.268	0.072	-1.297	-0.247	-2.880	0.004			_		
	Rudolph, 2009	-0.572	0.248	0.061	-1.057	0.086	-2.309	0.021		20 - 10 - 10 - 10 - 10 - 10 - 10 - 10 -			
		-0.576	0.105	0.011	-0.782	-0.370	-5.481	0.000		- 1	8		
									2.00	-1.00	0.00	1.00	2.0
Cognition: MMSE only	Study name	Difference	_s Standard	tatistics for	r each st Lower	tudy Upper				Differenc	e in means	and 95% Cl	
		in means	error	Variance	limit	limit	Z-Value	p-Value					
	Caldas, 2019	-4.627	1.226	1.503	-7.030	-2.224	-3.774	0.000	I —			I	1
	Chen, 2017	-0.200	0.116	0.013	-0.428	0.028	-1.722	0.085			pi -		
	Oldham, 2018	-0.900	0.482	0.232	-1.845		-1.867	0.062		.	-∎-Ī		
	Al Tmimi, 2016	0.000	0.394	0.155	-0.773	0.773	0.000	1.000			-#-		
	Li, 2015	-3.300	1.611	2.595	-6.457	-0. 143	-2.048	0.041	-		—T		
	Oldham, 2015	-1.600	0.587	0.344	-2.750	-0.450	-2.726	0.006			∎		
	Rudolph, 2009	-1.400	0.594	0.353	-2.565	-0.235	-2.356	0.018			◼─│		
		-1.136	0.394	0.155	-1.907	-0.364	-2.884	0.004		•	$\bullet$		
									-8.00	-4.00	0.00	4.00	8
Depression GDS	Study name			Statistics	for each	study				Differen	ce in means	and 95% CI	2
		Difference	Standard		Lowe	r Uppe	er						
		in means	error	Variance				ue p-Value					
	Oldham, 2018	1.000	0.599	0.359	-0.1	74 2.1	74 1.6	69 0.095	a 1	1	_		
									2		5		
	Oldham, 2015	0.400	0.716						00				Sel Marines
		0.753	0.459	0.211	-0.14	48 1.6	1.6	39 0.101	34	201	-	a di si se	
									-2.00	- <mark>1.0</mark> 0	0.00	1.00	2.0
Education (years)	Charles and a second			Charline			_			0.46			
Education (years)	Study name	1222	2011-017	Statistics	Constant Street					Differen	ce in means	and 95% CI	
		Difference in means	Standard	l Varianc	e lim			lue p-Value					
								Stor Wardenage	1.000	1.12	1	- F	T T
	Caldas, 2019	-1.38						808 0.419					
	Kazmierski, 2014c	-1.76						206 0.001					
	Kazmierski, 2014b	-1.22						388 0.165					1.1
	LI, 2015	1.30						568 0.570			1.1	•	े
	Mu, 2010	0.00						000 1.000				-	
	Otomo, 2013	-1.00						337 0.181					
		-0.92	6 0.37	0 0.13	57 -1.0	652 -0	.200 -2.	499 0.012	÷ 1			46	1
									-4.00	-2.00	0.00	2.00	4.0
EuroSCORE	Study name			Statistics fo	or each s	study				Differe	ence in means	and 95% CI	
		Difference in means	Standard error	Variance	Lower limit	Upper limit	7.Value	p-Value		05			
	Al Tmimi, 2016								1	315	1-	1	1
	Caldas, 2019	0.305	0.248	0.061	-0.180		1.233	0.218					
	Dong, 2014	0.500	0.198	0.039	0.111			0.012					
	Lopanen, 2008	1.800	0.771	0.594	0.289			0.020					
	Martin, 2012	5.600	0.442	0.196	4.733	6.467	12.664	0.000			8		>
	Mu, 2010	1.200	0.251	0.063	0.708			0.000				■-	
	Narkeine, 2007	1.700	0.379	0.143	0.958			0.000					
		0.000	0.542	0.294	-1.062	1.062		1.000		8	-	1	
	Ringaitiene, 2015		14433	2012023	108.202								
	Sev uk, 2015	0.010	0.042	0.002	-0.073			0.814					
		0.010 1.690	0.315	0.100	1.072	2.308	5.357	0.000					
	Sev uk, 2015	0.010				2.308	5.357		-4.00	-2.00	0.00	2.00	4.

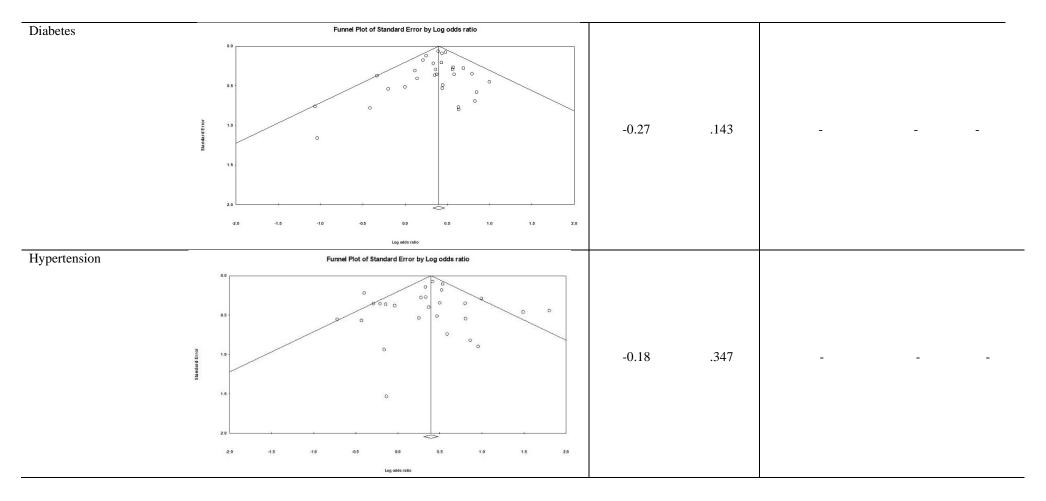
LVEF(%)	Study name		<u></u>	Statistics f	oreach s	tudy				Difference in means and 95% CI
		Difference	Standard	Magina	Lower	Upper	7.1/-	n Mahar		
	0-14 2040	in means	error	Variance	limit	limit	Z-Value			<b>H</b> 11 1
	Caldas, 2019 Chen, 2017	-3.577 2.300	1.461	2.133	-6.440 -0.948	-0.714 5.548	-2.449 1.388	0.014	ÉA)	
	Kazmierski, 2014c	-0.054	1.882	3.540	-3.742		-0.029	0.103		
	Kazmierski, 2014b	0.398	2.292	5.255	-4.096	4.891	0.173	0.862		
	Khan, 2014	-2.490	0.870	0.756	-4.194	-0.786	-2.863	0.004		
	Mardani, 2012	0.120	0.922	0.849	-1.686	1.926	0.130	0.896		
	Mu, 2010	2.700	1.222	1.492	0.306	5.094	2.210	0.027		
	Norkeine, 2007	6.700	1.455	2.118	3.848	9.552	4.604	0.000		
	Ringaitiene, 2015 Rudolph, 2009	3.900 1.000	2.524 2.426	6.372 5.887	-1.047 -3.756	8.847 5.756	1.545	0.122		
	Santana Santos, 2004	4.000	1.725	2.975	0.619	7.381	2.319	0.020		
		1.247	0.990	0.979	-0.692		1.260	0.208		
									-8.00	4.00 0.00 4.00
Intra-Operative (Continuous)										
ACC time (mins)	Study name			Statistics					<u> </u>	Difference in means and 95% CI
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value		
	Caldas, 2019	-13.00	6.766	45.776	-26.261	0.261	-1.921	0.055	<b>k</b> ∎	<b>⊢</b> ∔
	Leenders, 2018	6.10					2.348	0.019		
	Cumurcu, 2008 Eriksson, 2002	18.94 4.30					2.312 0.814	0.021 0.415		
	Kazmierski, 2014a	4.01					1.552	0.121		
	Kazmierski, 2014b	5.53					2.047	0.041		
	Khan, 2014	28.22	0 2.004	4.017	24.292	32.148	14.081	0.000		10405
	Loponen, 2008	8.00					1.173	0.241		
	Mardani, 2012 Mariscalco, 2012	2.00 19.80					0.917	0.359		1
	Nikolic, 2012	1.17					0.479	0.632		
	Norkeine, 2007	3.10					0.918	0.359		
	Ringaitiene, 2015	-5.50					-0.796	0.426	<del>30</del>	
	Santana Santos, 2004 Sevuk, 2015	2.04					0.570	0.569 0.816		
	Tully, 2010	8.10				15.929	2.028	0.043		
		5.97	0 2.732	2 7.462	0.616	11.324	2.185	0.029	-20.00	-10.00 0.00 10.00 2
(DD time (mine)	Study name		SI	alistics for	ach stud	W.			n	ffemore in means and 95% Cl
CPB time (mins)	Study name	Difference	St	atistics for a		-			D	ifference in means and 95% CI
CPB time (mins)		in means	Standard error V	L /ariance	ower U limit	pper limit Z-	31.02 22	/alue		ifference in means and 95% CI
CPB time (mins)	Caldas, 2019	in means -7.000	Standard error V 7.878	L Aariance 62.035 -3	ower U limit 2.437	pper limit Z- 8.437	0.889	0.374		ifference in means and 95% CL
CPB time (mins)	Caldas, 2019 Cumurou, 2008	in means -7.000 15.260	Standard error V 7.878 8.490	L Ariance 62.035 - 4 72.077	ower U limit 1 2.437 1.380 3	pper limit Z- 8.437 1.900	0.889 1,797	0.374 0.072	_	Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019	in means -7.000	Standard error V 7.878	L Ariance 62.035 - 4 72.077	ower U limit 1 2.437 1.380 3 0.374 2	pper limit Z- 8.437 1.900 8.174	0.889 1.797 0.905	0.374		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002	in means -7.000 15.260 8.900	Standard error V 7.878 8.490 9.834	4ariance 62.035 -3 72.077 96.701 -1 3.695	ower U limit 2.437 1.380 3 0.374 2 1.333	pper limit Z- 8.437 1.900 8.174 8.857	0.889 1.797 0.905 2.653	0.374 0.072 0.365	_	Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002 Gottesman, 2010 Kazmierski, 2014a Kazmierski, 2014b	-7.000 15.260 8.900 5.100 12.660 15.349	Standard error V 7.878 8.490 9.834 1.922 3.839 4.968	Aariance 62.035 -2 72.077 96.701 -1 3.695 14.740 24.663	ower U limit 2.437 1.380 3 0.374 2 1.333 5.135 2 5.615 2	pper limit Z- 8.437 1.900 8.174 8.867 0.184 5.082	0.889 1.797 0.905 2.653 3.297 3.091	0.374 0.072 0.365 0.008 0.001 0.002		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikason, 2002 Gottesman, 2010 Kazmierski, 2014a Kazmierski, 2014b Khan, 2014	-7.000 15.260 8.900 5.100 12.660 15.349 2.100	Standard error V 7.876 8.490 9.834 1.922 3.839 4.968 3.318	Ariance 62.035 -2 72.077 96.701 -1 3.695 14.740 24.663 10.995	ower U limit 2.437 1.380 3 0.374 2 1.333 5.135 2 5.615 2 4.399	pper limit Z- 1.900 8.174 8.867 0.184 5.082 8.599	0.889 1.797 0.905 2.653 3.297 3.091 0.633	0.374 0.072 0.365 0.008 0.001 0.002 0.527		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002 Gottesman, 2010 Kazmierski, 2014a Kazmierski, 2014b	-7.000 15.260 8.900 5.100 12.660 15.349	Standard error V 7.876 8.490 9.834 1.922 3.839 4.966 3.316 5.346	Ariance 62.035 -2 72.077 - 96.701 -1 3.695 14.740 24.663 10.995 28.576	ower U limit 2.437 1.380 3 0.374 2 1.333 5.135 2 5.615 2 4.399	pper limit Z- 8.437 1.900 8.174 8.807 0.184 5.082 8.699 1.241	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143	0.374 0.072 0.365 0.008 0.001 0.002		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikason, 2002 Gotteaman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008	in means -7.000 15.260 8.900 5.100 12.660 15.349 2.100 0.764 46.200 10.000	Standard error V 7.878 8.490 9.834 1.922 3.839 4.968 3.318 5.346 45.417 2 7.903	Aariance 62.035 -2 96.701 -1 3.695 14.740 24.663 10.995 28.576 062.711 -4 62.462	ower U limit 2.437 1.380 3 0.374 2 1.333 5.135 2 5.615 2 4.399 8.713 1 2.816 13 5.490 2	pper innit Z- 8.437 1.900 8.174 8.887 0.184 5.082 8.599 1.241 5.216 5.490	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265	0.374 0.072 0.365 0.008 0.001 0.002 0.527 0.886 0.309 0.206		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardani, 2012	in means -7.000 15.260 8.900 5.100 12.660 15.349 2.100 0.764 46.200 10.000 2.000	Standard error V 7.878 8.490 9.834 1.922 3.839 4.988 3.318 5.348 45.417 2 7.903 3.442	Aariance 82.035 -3 72.077 -9 96.701 -1 3.695 14.740 24.663 10.995 28.576 082.711 -4 82.462 11.847	ower U limit 2.437 1.380 3 0.374 2 1.333 5.135 2 5.615 2 4.399 9.713 1 2.816 13 5.490 2 4.746	pper innit Z- 8.437 1.900 8.174 8.887 0.184 5.082 8.599 1.241 5.218 5.490 8.746	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265 0.581	0.374 0.072 0.385 0.008 0.001 0.002 0.527 0.886 0.309 0.208 0.561	-	Ifference in means and 95% Cl
CPB time (mins)	Caldas. 2019 Cumurau, 2008 Erikesona, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardiani, 2012 Mariscalco, 2012	in means -7.000 15.260 8.900 5.100 12.860 15.349 2.100 0.764 46.200 10.000 2.000 25.700	Standard error V 7.876 8.490 9.834 1.922 3.839 4.966 3.316 5.346 45.417 2.7.903 3.442 4.450	Aariance 62.035 -2 72.077 -9 96.701 -1 3.695 14.740 24.663 10.995 28.576 062.711 -4 62.462 11.847 19.799 1	ower         U           limit         2.437           1.380         3           0.374         2           1.333         5.135           5.135         2           4.399         9.713           9.713         1           2.816         13           5.490         2           4.746         6.979	Der innit Z- 8.437 - 1.900 8.174 8.887 0.184 5.082 8.599 1.241 5.216 5.490 8.746 4.421	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265 0.581 5.776	0.374 0.072 0.365 0.008 0.001 0.002 0.527 0.886 0.309 0.206 0.561 0.000		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2014 Li, 2015 Loponen, 2008 Mardani, 2012 Marisoaloo, 2012 Nikolic, 2012	in means -7.000 15.200 8.900 5.100 12.860 15.349 2.100 0.784 48.200 10.000 2.5.700 9.073	Standard error V 7.876 8.490 9.834 1.922 3.839 4.968 3.316 5.346 45.417 2 7.903 3.442 4.450 3.045	Ariance 62.035 - 72.077 - 96.701 - 14.740 14.740 10.995 - 28.576 062.711 - 11.847 - 11.847 - 19.799 1 9.272	owner         U           limit         1.380         3           1.380         3         0.374         2           1.333         5.135         2         5.615         2           4.399         9.713         1         2         816         13           5.430         2         8.16         13         5         4.99         2           4.746         6.979         3         3.105         1         3         10         1	pper iminit Z: 8.437 1.900 8.174 8.887 0.184 5.082 8.899 1.241 5.216 8.490 8.746 4.421 5.041	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265 0.581 5.776 2.980	0.374 0.072 0.365 0.008 0.001 0.002 0.527 0.886 0.309 0.206 0.561 0.000 0.003		Ifference in means and 95% CI
CPB time (mins)	Caldas. 2019 Cumurau, 2008 Erikesona, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardiani, 2012 Mariscalco, 2012	in means -7.000 15.260 8.900 5.100 12.860 15.349 2.100 0.764 46.200 10.000 2.000 25.700	Standard error V 7.876 8.490 9.834 1.922 3.839 4.966 3.316 5.346 45.417 2.7.903 3.442 4.450	Ariance 62.035 - 72.077 - 96.701 - 14.740 14.740 10.995 - 28.576 062.711 - 11.847 - 11.847 - 19.799 1 9.272	owner         U           limit         2.437           1.380         3           0.374         2           1.333         5.135           5.615         2           4.399         9.713           9.713         1           2.816         13           5.490         2           4.746         6.979           3.105         1           0.096         2	pper ismit Z: 8.437 1.900 8.174 8.887 0.184 5.082 8.899 1.241 5.216 5.490 8.746 4.421 5.041 3.696	0.889 1.797 0.905 2.853 3.297 3.091 0.833 0.143 1.017 1.265 0.581 5.776 2.980 1.944	0.374 0.072 0.365 0.008 0.001 0.002 0.527 0.886 0.309 0.206 0.561 0.000		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikason, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2014b Li, 2015 Loponen, 2008 Mardani, 2012 Marisaaloo, 2012 Nikolio, 2012 Norkeine, 2007 Oldham, 2018 Otomo, 2013	in means -7,000 15,260 8,900 12,860 15,349 2,100 0,764 46,200 10,000 2,000 2,5,700 9,073 11,800 -3,000 21,000	Standard error V 7.876 8.490 9.834 1.922 3.839 4.966 3.316 5.346 4.547 4.547 7.903 3.442 4.547 3.045 6.089 9.730 16.018	L         L           62.035         -72.077           98.701         -13.695           3.695         -14.740           24.663         10.996           28.576         -082.711           -082.711         -4.624           11.847         -9.272           36.837         -94.681           94.681         -256.565	owner         U           1amit         1.380         3           1.380         3         0.374         2           1.333         5.135         2         5.615         2           4.399         9.713         1         2.816         13           5.439         2.816         13         5.490         2           4.746         6.979         3         3.105         1           0.096         2         2.071         1         0.394         5	- pper limit Z- 8.437 1.900 8.174 8.887 0.184 5.082 8.599 1.241 5.216 5.490 8.746 4.421 5.041 3.696 6.071 2.394	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.043 1.017 1.265 0.581 5.776 2.980 1.944 0.308 1.311	0.374 0.072 0.365 0.008 0.001 0.002 0.527 0.888 0.309 0.208 0.561 0.000 0.003 0.652 0.552 0.552 0.552 0.552 0.552 0.552 0.552 0.552 0.552 0.552 0.552 0.552		Ifference in means and 35% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikason, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardani, 2012 Mariacalco, 2012 Nikolic, 2012 Nikolic, 2012 Nikolic, 2013 Ringaifene, 2015	in means -7.000 15.260 8.900 5.100 12.660 15.349 2.100 0.764 48.200 10.000 2.000 2.000 2.000 2.5.700 9.073 11.800 -3.000 2.1.000 -3.000 2.1.000 -3.000 -3.000 -3.000 -0.0000 -0.0000 -0.0000 -0.000 -0.000	Standard error V 7.878 8.490 9.834 1.922 3.839 4.988 4.989 3.316 5.346 4.5417 2.7.903 3.442 4.4503 3.045 6.089 9.730 10.099	Aariance 62.035 - 372.077 - 96.701 - 3.695 - 14.740 - 24.683 - 14.740 - 24.683 - 28.576 - 062.711 - 46.2462 - 11.847 - 19.799 - 19.272 - 36.837 - 94.681 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.565 - 1116.611 - 3.256.5555 - 3.256.555 - 3.256.555 - 3.256.555 - 3.256.555 - 3.256.5555 - 3.256.5555 - 3.256.5555 - 3.256.5555 - 3.256.5555 - 3.256.5555 - 3.256.5555 - 3.25655555555555555555555555555555555555	owner         U           limit         1.380           1.380         3           0.374         2           1.333         5.135           5.135         2           4.399         9.713           9.713         1           2.816         13           5.490         2           4.746         6.979           0.096         2           2.071         1           0.096         2           2.071         1           0.394         5	Ppper limit Z- 8.437 1.900 8.174 8.807 0.184 5.082 8.599 1.241 5.216 8.490 8.746 4.421 5.041 3.696 6.071 2.394 1.065	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265 0.581 5.776 2.980 1.944 0.308 1.311 0.009	0.374 0.072 0.385 0.001 0.002 0.527 0.888 0.309 0.208 0.561 0.000 0.003 0.052 0.561 0.003 0.052 0.758 0.758 0.190		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikeson, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardani, 2012 Nisolic, 2012 Nisolic, 2012 Nisolic, 2012 Nisolic, 2013 Ringališene, 2015 Rudolph, 2009	in means -7.000 15.260 8.900 5.100 12.660 15.349 2.100 0.764 46.200 10.000 2.000 25.700 9.073 11.800 -3.000 21.000 -0.000 2.000	Standard error V 7.878 8.490 9.834 1.922 3.839 4.968 3.316 5.346 4.5417 7.903 3.442 4.450 3.045 6.089 9.730 18.018 6.089 9.730 10.799	Aariance 62.035 - 372.077 - 3.695 - 3.695 - 3.695 - 14.740 - 24.863 - 28.576 - 062.711 - 4 - 65.576 - 062.711 - 4 - 62.462 - 36.837 - 36.8	ower         U           limit         1.380           1.380         3           0.374         2           1.383         3           5.135         2           4.399         9           9.713         1           2.816         13           5.476         6           6.979         3           3.105         1           0.096         2           2.071         1           0.394         5           1.285         1	- pper limit Z- 8.437 1.900 8.174 5.082 8.887 0.184 5.082 8.899 8.746 4.421 5.041 3.696 6.071 2.394 5.041 3.696 5.041	0.889 1.797 0.905 2.653 3.297 0.633 0.143 1.017 1.265 2.980 1.944 0.581 5.776 2.980 1.944 0.009 0.294	0.374 0.072 0.865 0.008 0.001 0.002 0.827 0.888 0.309 0.208 0.561 0.003 0.052 0.003 0.052 0.758 0.993 0.993		Ifference in means and 95% CI
CPB time (mins)	Caldas, 2019 Cumurou, 2008 Erikason, 2002 Gottesman, 2010 Kazmierski, 2014a Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardani, 2012 Mariacalco, 2012 Nikolic, 2012 Nikolic, 2012 Nikolic, 2013 Ringaifene, 2015	in means -7.000 15.260 8.900 5.100 12.660 15.349 2.100 0.764 48.200 10.000 2.000 2.000 2.000 2.5.700 9.073 11.800 -3.000 2.1.000 -3.000 2.1.000 -3.000 -3.000 -3.000 -0.0000 -0.0000 -0.0000 -0.000 -0.000	Standard error V 7.878 8.490 9.834 1.922 3.839 4.988 4.989 3.316 5.346 4.5417 2.7.903 3.442 4.4503 3.045 6.089 9.730 10.099	L         L           62.035         -           72.077         -           96.701         -           3.695         -           14.740         -           24.863         -           28.576         -           062.711         -           62.462         -           11.847         -           19.799         1           9.272         -           28.636         -           118.47         -           19.799         1           226.636         -           116.611         -           46.158         -           27.873         -	ower         U           limit         1.380           2.437         1.380           1.380         3           5.135         2           5.615         2           4.399         9.713           9.713         1           2.816         13           5.490         2           4.746         6.979           6.979         3           3.108         1           0.096         2           2.071         1           0.394         5           1.265         2           1.316         1           6.378         1	- pper limit Z- 8.437 1.900 8.174 5.082 8.895 1.241 5.216 5.216 5.216 5.216 5.216 5.216 5.216 5.216 5.2490 8.746 4.421 3.696 6.071 2.394 4.021 3.696 6.071	0.889 1.797 0.905 2.853 3.297 3.091 0.833 0.143 1.017 1.265 0.581 5.776 2.980 1.944 0.308 1.311 0.0294 0.294 0.752	0.374 0.072 0.385 0.001 0.002 0.527 0.888 0.309 0.208 0.561 0.000 0.003 0.052 0.561 0.003 0.052 0.758 0.758 0.190		Ifference in means and 95% CI
CPB time (mins)	Caldas. 2019 Cumurau, 2008 Erikaon, 2002 Gottesman, 2010 Kazmierski, 2014a Kazmierski, 2014b Khan, 2014 Leenders, 2018 Li, 2015 Loponen, 2008 Mardani, 2012 Mariscalco, 2012 Nikolic, 2012 Nikolic, 2012 Nikolic, 2013 Ringaitene, 2015 Rudolph, 2009 Santana Santos, 2004	in means -7.000 15.260 8.900 12.660 15.349 2.100 0.764 46.200 10.000 2.5.700 9.073 11.800 2.1.000 -3.000 21.000 2.1.000 3.970	Standard error V 7.878 8.490 9.834 1.922 3.839 4.968 3.316 5.346 5.346 5.346 5.346 5.346 5.346 5.346 5.346 5.346 5.069 9.730 3.045 6.069 9.730 16.018 10.799 6.794 5.294	Lariance         Cariance           62.035         72.077           72.077         3.695           14.740         24.683           28.576         002.711           02.462         11.847           19.799         9.272           26.837         94.681           205.056         11.641           205.056         116.611           40.156         -127.873           24.492         -24.492	ower         U           limit         1.380           1.380         3           1.333         5.135           5.135         2           4.399         9.713           9.713         1           2.816         13           5.435         2           4.746         6.979           6.979         3           0.096         2           2.071         1           0.394         5           1.1285         2           1.316         1           6.378         1           2.889         4	Pper imit Z. 8.437 1.900 8.174 8.807 0.184 5.082 8.509 1.241 5.216 8.490 8.746 4.421 3.696 8.746 4.421 3.696 8.071 2.394 4.318 5.316 4.318 9.982 2.889	0.889 1.797 0.905 2.653 3.297 3.091 0.633 0.143 1.017 1.265 0.581 1.944 0.308 1.944 0.308 0.294 0.752 0.057 1.713	0.374 0.072 0.865 0.000 0.001 0.001 0.002 0.527 0.886 0.309 0.206 0.561 0.003 0.052 0.758 0.993 0.768 0.993 0.768		Ifference in means and 95% CI

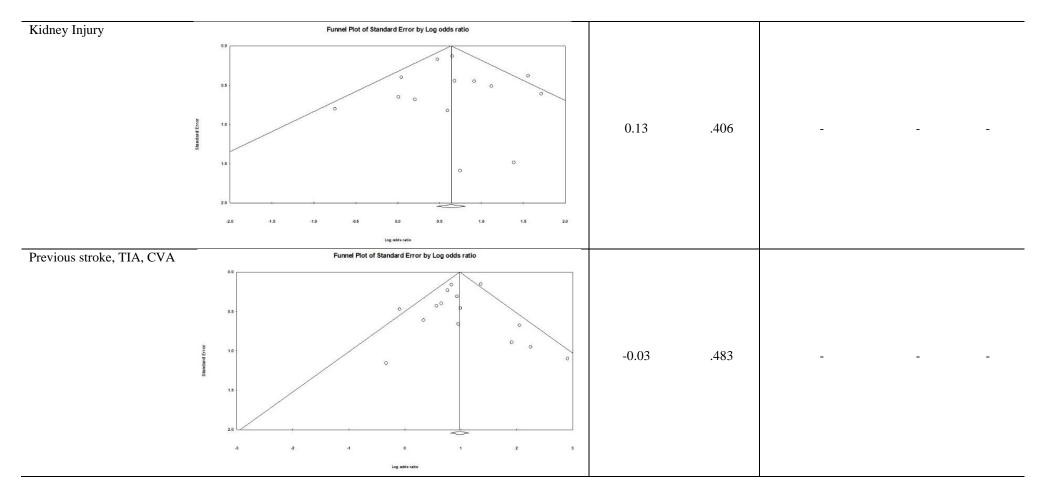
Duration of surgery (mins)	Study name	0.22	C4- 1	Statistics for	135	1000				Differenc	ce in means and 95% CI
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value			
	Caldas, 2019	-20.000	16. <mark>44</mark> 7	270.493	-52.235	12.235	-1.216	0.224	k-		
	Dong, 2014 Kazmierski, 2014a	30.000 30.000	11.195 8.930	125.329 79.753	8.058 12.497	51.942 47.503	2.680 3.359	0.007			
	Kazmierski, 2014b	40.683	9.203	84.688	22.646	58.720	4.421	0.000			
	Mu, 2010	22.800	8.817	77.741	5.519	40.081	2.586	0.010			
	Nikolic, 2012 Norkeine, 2007	43.510 32.000	10.354 15.245	107.195 232.396	23.218 2.121	63.803 61.879	4.202	0.000			
	Oldham, 2018	0.000	14.076	198.142	-27.589	27.589	0.000	1.000		100	<b>+</b> +^
	Otomo, 2013	9.000	22.941	526.310	-35.964	53.964	0.392	0.695			
	Ringaitiene, 2015 Rudolph, 2009	5.400 -2.000	16.955 14.265	287.464 203.477	-27.831 -29.958	38.631 25.958	0.318	0.750			
	Sevuk, 2015	2.100	4.524	20.462	-6.766	10.966	0.464	0.642			-
	Zhang, 2015	48.070	8.779	77.073	30.863	65.277	5.475	0.000			
		20.526	6.048	36.574	8.673	32.379	3.394	0.001	-50.00	-25.00	0.00 25.00
										2000	0.00
Intubation time (hours)	Study name		S	tatistics for	each stu	dy				Difference	e in means and 95% Cl
()		Difference sin means	Standard error	Variance		Upper	Z-Value	p-Value			
	Al Tmimi, 2016	5.088	1.919	3.684	limit 1.326	limit 8.850	2.651	0.008	Ť	T	1
	Eriksson, 2002	0.200	1.423	2.024	-2.588	2.988	0.141	0.888			_ <b>+</b> ₽
	Khan, 2014	11.680	0.683	0.467	10.341	13.019	17.100	0.000			■
	Mariscalco, 2012 Mu, 2010	31.918 2.311	1.457	2.123	29.062 1.343	34.774 3.279	21.907 4.677	0.000			
	Nikolic, 2012	0.375	2.767	7.657	-5.049	5.799	0.135	0.892		0	<b>#</b>
	Norkeine, 2007	4.150	1.176	1.383	1.845	6.455	3.528	0.000			
	Otomo, 2013	2.000	2.089	4.363	-2.094	6.094	0.957	0.338			
	Sevuk, 2015 Siepe, 2011	0.360	0.368 2.181	0.136 4.755	-0.362	1.082	0.978	0.328			T
	Zhang, 2015	10.428	1.740	3.028	7.018	13.839	5.992	0.000			
		6.820	2.234	4.990	2.442	11.199	3.053	0.002		l,	
									-20.00	-10.00	0.00 10.00
Number of grafts	Study name			tatistics for	each stu					Difform	a in means and 95% Cl
Number of grafts	Study name	Difference S	 Standard	tatistics for		Upper				Difference	ce in means and 95% Cl
		in means		Variance	limit		Z-Value	p-Value			
	Dong, 2014	0.200	0.206	0.042	-0.204	0.604	0.971	0.332		1	
	Loponen, 2008	0.300	0.292	0.085	-0.272	0.872	1.028	0.304			
	Mardani, 2012 Mu, 2010	-0.190	0.126	0.016	-0.437 -0.089	0.057	-1.506 1.038	0.132		2.5	
	Norkeine, 2007	0.210	0.169	0.029	-0.122	0.542	1.240	0.215			
	Rudolph, 2009	0.200	0.163	0.027	-0.119	0.519	1.228	0.220			+
	Sevuk, 2015	0.296	0.112	0.013	0.076	0.516	2.633	0.008		22	
	Zhang, 2015	-0.036	0.147	0.022	-0.324	0.252	-0.246	0.806			
		0.111	0.064	0.004	-0.015	0.237	1.730	0.084	-1.00	-0.50	0.00 0.50
									-1.00	-0.00	0.00 0.50
Post-Operative (Categorical)											
	_										
Arrhythmia, incl. AF	Study nar	ne		Statis	tics fo	reach	study			Odds	ratio and 95% Cl
•			Odd	s Lowe b limit			/alue r	-Value			
							CREW CONTRACT		80	1 1	· · · · ·
	Caldas 20	010		1 1 16	2 15 2	nn	2506				
	Caldas, 20		4.71		2 15.2		2.596	0.009			
	Coffey, 19	983	4.71 6.77	71 3.13	6 14.6	619	4.871	0.000			
	Coffey, 19 Cumurcu,	983 2008	4.71 6.77 3.30	71 3.13 00 0.71	6 14.6 8 15.1	619 4 162 -	4.871 1.535	0.000 0.125			
	Coffey, 19 Cumurcu, Eriksson,	983 2008 2002	4.71 6.77 3.30 1.00	71 3.13 00 0.71 00 0.22	6 14.6 8 15.1 5 4.4	619 62 436 (	4.871 1.535 0.000	0.000 0.125 1.000			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersł	983 2008 2002 ti, 2014a	4.71 6.77 3.30 1.00 9.51	71 3.13 00 0.71 00 0.22 17 2.49	6 14.6 8 15.1 5 4.4 8 36.2	619 62 436 254	4.871 1.535 0.000 3.302	0.000 0.125 1.000 0.001			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Kazmiersk	983 2008 2002 si, 2014a si, 2014b	4.71 6.77 3.30 1.00 9.51 4.39	71 3.13 00 0.71 00 0.22 17 2.49 04 1.07	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8	619 62 436 254 393	4.871 1.535 0.000 3.302 2.066	0.000 0.125 1.000 0.001 0.039			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Kazmiersk Loponen,	983 2008 2002 xi, 2014a xi, 2014b 2008	4.71 6.77 3.30 1.00 9.51 4.39 4.72	71 3.13 00 0.71 00 0.22 17 2.49 94 1.07 22 1.51	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7	519     4       162     1       136     0       254     1       393     1       711     1	4.871 1.535 0.000 3.302 2.066 2.677	0.000 0.125 1.000 0.001 0.039 0.007		-	
	Coffey, 19 Cumurcu, Eriksson, Kazmiersł Kazmiersł Loponen, Mardani, 2	983 2008 2002 di, 2014a di, 2014b 2008 2012	4.71 6.77 3.30 1.00 9.51 4.39 4.72 2.17	71         3.13           00         0.71           00         0.22           17         2.49           94         1.07           22         1.51           76         0.90	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7 2 5.2	319     4       162     4       136     0       254     3       393     2       711     2	4.871 1.535 0.000 3.302 2.066 2.677 1.730	0.000 0.125 1.000 0.001 0.039 0.007 0.084			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Kazmiersk Loponen, Mardani, 2 Mariscalc	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 co, 2012	4.71 6.77 3.30 1.00 9.51 4.39 4.72 2.17 3.17	71         3.13           00         0.71           00         0.22           17         2.49           04         1.07           22         1.51           76         0.90           78         2.07	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7 2 5.2 6 4.8	319     4       162     4       136     0       254     3       393     2       711     2       366     3	4.871 1.535 0.000 3.302 2.066 2.677	0.000 0.125 1.000 0.001 0.039 0.007			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersł Kazmiersł Loponen, Mardani, 2	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 co, 2012	4.71 6.77 3.30 1.00 9.51 4.39 4.72 2.17	71         3.13           70         0.71           70         0.22           17         2.49           94         1.07           72         1.51           76         0.90           78         2.07           73         1.26	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7 2 5.2 6 4.8 6 2.8	319     4       162     4       436     0       254     3       393     2       711     2       366     4       363     3	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320	0.000 0.125 1.000 0.001 0.039 0.007 0.084 0.000			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Kazmiersk Loponen, Mardani, 2 Mariscalco Miy azaki, Mu, 2010	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 c, 2012 2011	4.7 <sup>4</sup> 6.77 3.30 1.00 9.5 <sup>5</sup> 4.39 4.72 2.17 3.17 1.90 2.7 <sup>4</sup>	71         3.13           70         0.71           90         0.71           90         0.22           17         2.49           94         1.07           92         1.51           76         0.90           78         2.07           93         1.26           18         0.93	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7 2 5.2 6 4.8 6 2.8 8 7.8	319     4       162     436       436     93       254     393       211     2       366     4       363     3       377     3	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091 1.842	0.000 0.125 1.000 0.001 0.039 0.007 0.084 0.000 0.002			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Loponen, Mardani, 2 Mariscalco Miy azaki, Mu, 2010 Nikolic, 20	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 0, 2012 2011 2011	4.7 <sup>4</sup> 6.77 3.30 1.00 9.5 <sup>5</sup> 4.39 4.72 2.17 3.17 1.90 2.7 <sup>4</sup> 1.6 <sup>4</sup>	71         3.13           70         0.71           70         0.22           17         2.49           74         1.07           72         1.51           76         0.90           78         2.07           73         1.26           18         0.93           16         0.95	6 14.6 8 15.1 5 4.4 8 36.2 9 17.8 6 14.7 2 5.2 6 4.8 6 2.8 8 7.8	619     4       162     436       1436     0       254     3       393     2       711     2       366     4       363     3       377     7       735     5	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091	0.000 0.125 1.000 0.001 0.039 0.007 0.084 0.000 0.002 0.065			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Loponen, Mardani, 2 Mariscalcu Miyazaki, Mu, 2010 Nikolic, 20 Norkeine,	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 co, 2012 2011 2011 2007	4.7 <sup>4</sup> 6.77 3.30 1.00 9.5 <sup>5</sup> 4.39 4.72 2.17 3.17 1.90 2.7 <sup>4</sup> 1.6 <sup>2</sup>	71         3.13           00         0.71           00         0.22           17         2.49           904         1.07           22         1.51           76         0.90           78         2.07           03         1.26           18         0.93           16         0.95           08         8.48	6       14.6         8       15.1         5       4.4         8       36.2         9       17.8         6       14.7         2       5.2         6       2.8         8       7.8         5       2.7         5       30.9	319     4       162     4       436     0       254     3       393     2       711     2       247     3       366     2       377     7       735     959	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091 1.842 1.787	0.000 0.125 1.000 0.001 0.039 0.007 0.084 0.000 0.002 0.065 0.074			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Loponen, Mardani, 2 Mariscalcu Miyazaki, Mu, 2010 Nikolic, 20 Norkeine,	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 co, 2012 2011 2011 2007 Santos, 200	4.7 <sup>4</sup> 6.77 3.30 1.00 9.5 <sup>5</sup> 4.39 4.72 2.17 3.17 1.90 2.7 <sup>4</sup> 1.6 <sup>2</sup>	71         3.13           00         0.71           00         0.22           17         2.49           94         1.07           22         1.51           76         0.90           78         2.07           03         1.26           18         0.93           16         0.95           08         8.48           19         1.76	6       14.6         8       15.1         5       4.4         8       36.2         9       17.8         6       14.7         2       5.2         6       4.8         7.8       7.8         5       2.7         5       30.9         5       6.6	619     4       162     4       436     0       254     3       393     2       711     2       247     3       366     3       377     7       735     9       959     8       626     3	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091 1.842 1.787 3.436	$\begin{array}{c} 0.000\\ 0.125\\ 1.000\\ 0.001\\ 0.039\\ 0.007\\ 0.084\\ 0.000\\ 0.002\\ 0.065\\ 0.074\\ 0.000\\ \end{array}$			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Loponen, Mardani, 2 Mariscalcu Miyazaki, Mu, 2010 Nikolic, 20 Norkeine, Santana S Tamura, 2	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 0, 2012 2011 2011 2007 Santos, 200 019	4.7 <sup>4</sup> 6.77 3.30 9.5 <sup>4</sup> 4.33 4.72 2.17 3.17 1.90 2.7 <sup>4</sup> 1.6 <sup>2</sup> 16.20 14 3.4 <sup>4</sup>	71         3.13           00         0.71           00         0.22           17         2.49           94         1.07           22         1.51           76         0.90           78         2.07           03         1.26           18         0.93           16         0.95           08         8.48           19         1.76           40         0.26	6       14.6         8       15.1         5       4.4         8       36.2         9       17.8         6       14.7         2       5.2         6       4.8         7       5.2         6       2.8         7.5       30.9         5       6.6         9       4.0	319       4         162       4         436       0         2254       3         393       2         711       2         247       3         366       3         377       7         735       3         526       3         526       3         518       0	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091 1.842 1.787 8.436 3.642	$\begin{array}{c} 0.000\\ 0.125\\ 1.000\\ 0.001\\ 0.039\\ 0.007\\ 0.084\\ 0.000\\ 0.002\\ 0.065\\ 0.074\\ 0.000\\ 0.000\\ 0.000\\ \end{array}$			
	Coffey, 19 Cumurcu, Eriksson, Kazmiersk Loponen, Mardani, 2 Mariscalcu Miyazaki, Mu, 2010 Nikolic, 20 Norkeine, Santana S	283 2008 2002 ci, 2014a ci, 2014b 2008 2012 0, 2012 2011 2011 2007 Santos, 200 019	4.7 <sup>4</sup> 6.77 3.30 9.5 <sup>4</sup> 4.32 4.72 2.11 3.17 1.90 2.7 <sup>4</sup> 1.6 <sup>2</sup> 16.20 14 3.4 <sup>4</sup>	71         3.13           00         0.71           00         0.22           17         2.49           94         1.07           22         1.51           76         0.90           78         2.07           03         1.26           18         0.93           16         0.95           08         8.48           19         1.76           40         0.26           04         2.86	6       14.6         8       15.1         5       4.4         8       36.2         9       17.8         6       14.7         2       5.2         6       4.8         7.8       7.8         5       2.7         5       30.9         5       6.6	319       4         162       4         436       0         254       3         393       2         711       2         247       3         366       3         377       7         735       9         959       8         526       3         518       0         780       4	4.871 1.535 0.000 3.302 2.066 2.677 1.730 5.320 3.091 1.842 1.787 8.436 3.642 0.057	0.000 0.125 1.000 0.001 0.039 0.007 0.084 0.000 0.002 0.065 0.074 0.000 0.000 0.000 0.955			

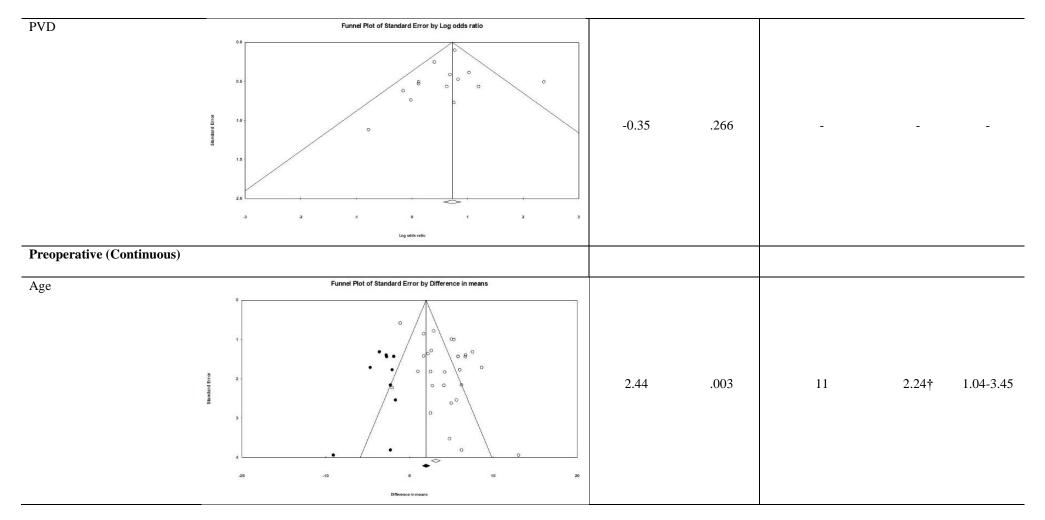
Post-Operative (Continuous)													
LOS in ICU (days)	Study name			Statistics for	or each st	tudy				Differenc	e in means	and 95% CI	
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
	Al Tmimi, 2016	1.491	0.339	0.115	0.826	2.155	4.396	0.000	1		1 4	- 1	1
	Caldas, 2019	2.910	1.833	3.361	-0.683	6.503	1.587	0.112			-		
	Chen, 2017	2.253	0.272	0.074	1.721	2.786	8.295	0.000			10.00	-	
	Eriksson, 2002	-0.100	0.209	0.044	-0.509	0.309	-0.479	0.632					
	Khan, 2014	6.510	0.234	0.055	6.052	6.968	27.852	0.000			10-00		>
	Mardani, 2012	0.530	0.251	0.063	0.037	1.023	2.108	0.035			-	20-22	
	Mariscalco, 2012	2.188	0.074	0.005	2.043	2.333	29.630	0.000					
	Mu, 2010	0.920	0.197	0.039	0.533	1.306	4.666	0.000					
	Norkeine, 2007	4.800	0.438	0.191	3.943	5.657	10.971	0.000					<b>-</b>
	Omiya, 2015	1.385	0.349	0.122	0.701	2.070	3.965	0.000			50	-	
	Palmbergen, 2012	2.990	0.385	0.148	2.236	3.744	7.773	0.000					
	Siepe, 2011	1.500	1.381	1.906	-1.206	4.206	1.087	0.277			8 <u>00</u>		
	Subramaniam, 2019	1.412	0.353	0.125	0.720	2.105	3.996	0.000			53 <u>51</u>	-	
	Zhang, 2015	2.500	0.311	0.097	1.890	3.110	8.035	0.000	1			-	
		2.221	0.462	0.213	1.316	3.126	4.812	0.000			0.0		
									-6.00	-3.00	0.00	3.00	6.

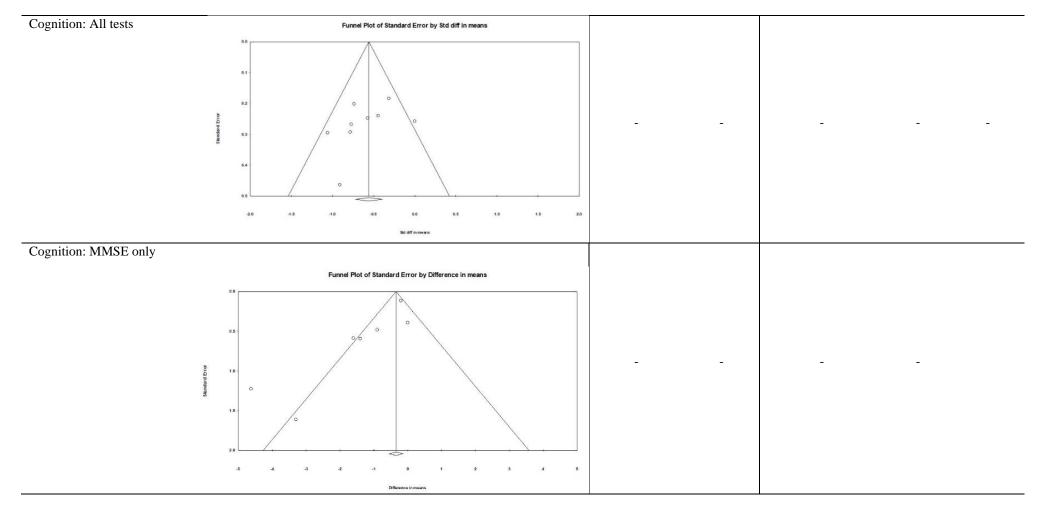


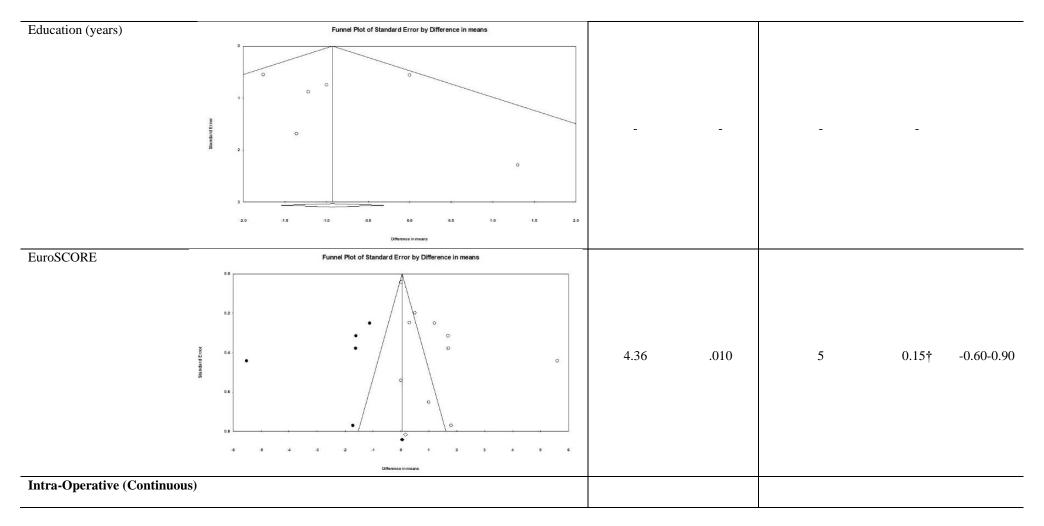


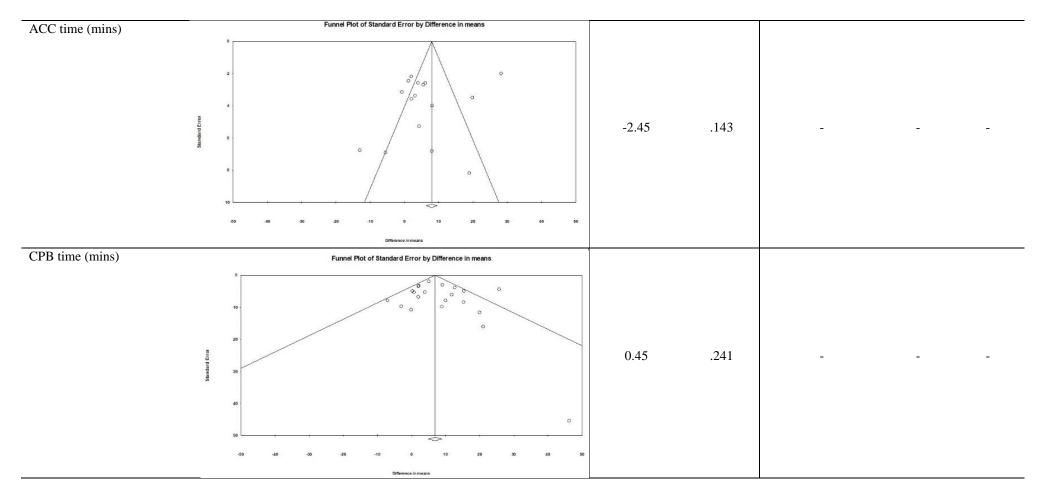


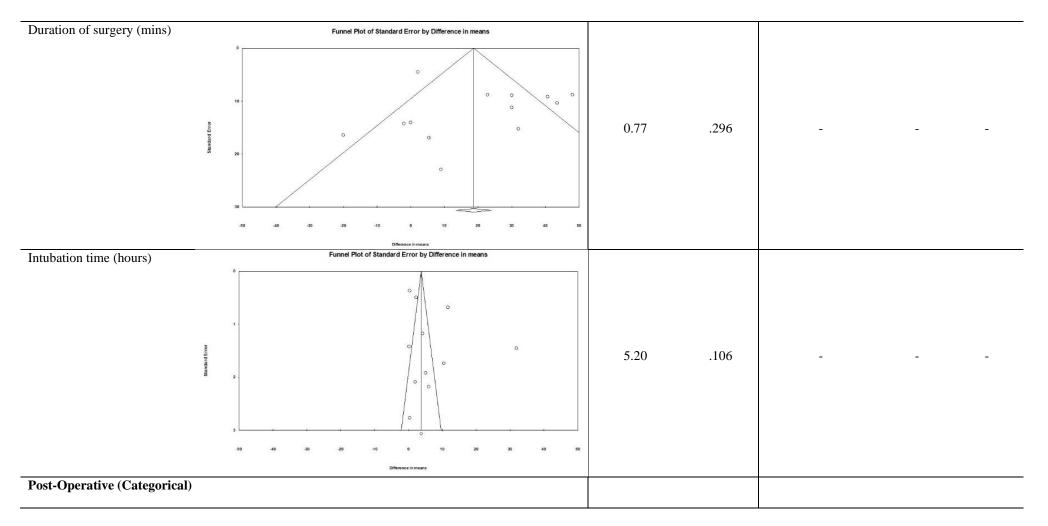












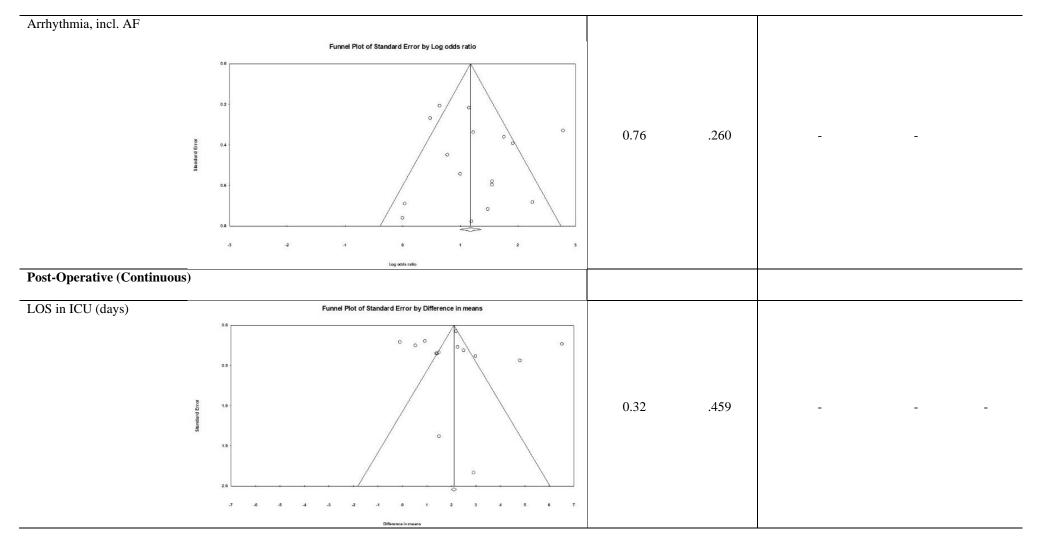


Figure S3. Forest	t plots for acute	cognitive decline	post-CABG analyses.

Variable	Forest Plot											
Pre-Operative (Categorical)												
Arrhythmia, incl. AF	Study name		Statisti	cs for ea	ach study			Od	ds ratio	and 95	% CI	
		Odds ratio	Lower limit		Z-Value	p-Value						
	Colak, 2015	11.000	1.425	84.927	2.299	0.021	T	1	- 10 - 1	1 +	-	1
	Dong, 2014	1.459	0.561	3.795	0.774	0.439				┼┲┼╴	-	
	Mu, 2013	0.938	0.397	2.214	-0.147	0.883			-			
	Norkiene, 2011	1.170	0.356	3.843	0.258	0.796			-		-	
	Restrepo, 2002	0.905	0.029	27.858	-0.057	0.954	k-	-			_	>
	Slater, 2009	0.495	0.056	4.360	-0.634	0.526	K-	_	-	+	_	
	Suksompong, 2002	1.090	0.216	5.504	0.104	0.917		-	-	╞┼	-+	
		1.243	0.757	2.041	0.861	0.389						
							0.1	0.2	0.5	1 2	5	10
Cognitive Impairment	Study name		Statistic	s for e	ach stud	y		Od	ds rati	o and 9	5% C	Ĺ
		Odds L ratio	ower limit		Z-Value	p-Value						
	Baba, 2007	0.752	0.161	3.504	-0.363		Í	+		•┼─┼	- I	
	Mu, 2013	1.241	0.463	3.329	0.430	0.668			-	╶┼═╾┼		
	Silbert, 2008	0.898	0.455	1.774	-0.309	0.757			-			
	Trubnikova, 2014	1 576	0.680	3.654	1.060				2			
		1.108	0.709	1.730	0.449							
		1.100	0.100	1.100	0.110	0.000	0.1	1 0.2	0.5	1 2	5	10
Depression	Study name	Sta	tistics	for eac	h study			Odd	s ratio	o and 9	5% CI	
	Od	ds Lov tio lin			-Value p	o-Value						
	Kadoi, 2011b 6.2		199 17		3.446	0.001	ľ	8		1 1-		
			791 4	.980	1.461	0.144						
			119 10	97999900	2.157	0.031						
								- S.	200		10100000000	6.00

Diabetes	Study name		Statisti	cs for ea	ch study	2	Odds ratio and 95% Cl
		Odds ratio	Lower limit		Z-Value	p-Value	
	Baba, 2007	1.148	0.570	2.312	0.387	0.698	
	Boodhwani, 2006	1.089	0.723	1.642	0.409	0.682	-#-
	Colak, 2015	1.149		2.176	0.427	0.669	
	deToumay-Jette, 2011	0.933		3.674	-0.099	0.921	
	Dong, 2014	2.810	1.151	6.860	2.268	0.023	
	Goto, 2000	1.717		4.299	1.155	0.248	
	Harmon, 2005	0.619		10.775	-0.329	0.742	
	Kadoi, 2005 Kumpaitiene, 2019	1.683	1.016	2.788	2.020	0.043 0.714	
	Mu, 2013	2.395	1.244	4.609	2.614	0.009	
	Norkiene, 2011	1.367		4.003	0.567	0.571	
	Oh, 2008	1.676	0.403	6.966	0.711	0.477	
	Reents, 2002	1.901		6.675	1.003	0.316	
	Restrepo, 2002	0.750		11.311	-0.208	0.835	
	Slater, 2009	0.834		1.442	-0.648	0.517	
	Suksompong, 2002	1.260		3.314	0.468	0.639	
	Toeg, 2013	1.950	1.391	2.733	3.878	0.000	-
		1.443	1.211	1.719	4.104	0.000	
							0.1 0.2 0.5 1 2 5 10
Dyslipidemia/Hyperlipidemia	Study name		Statist	ics for e	ach stud	ly	Odds ratio and 95% Cl
		Odds ratio	Lower limit		Z-Value	p-Value	
	Baba, 2007	1.079	0.539	2.161	0.214	0.830	1 1 1 🖛 1 1 1
	deTournay-Jette, 2011	0.630					
	Dong, 2014	1.071					
	Goto, 2000	0.719					
	Mu, 2013	1.038					
	Suksompong, 2002	4.730		14.371			
		1.164	0.739	1.835	0.655	0.512	0.1 0.2 0.5 1 2 5 10
Hypertension	Study name		Statist	ice for a	ach stud	hy.	Odds ratio and 95% Cl
	Study hame		Lower	Upper			
	D 1 0007	ratio	limit	limit		p-Value	
	Baba, 2007	0.929			-0.176		
	Colak, 2015	1.541					
	deTournay-Jette, 2011	4.000		15.895			
	Dong, 2014 Goto, 2000						
	Harmon, 2005	2.005					
	Kadoi, 2001	1.100		16.316			
	Kadoi, 2001	6.183		12.907			
	Kadoi, 2003	1.400					
	Kadoi, 2011b	2.059					
	Mu, 2013	2.283					
	Norkiene, 2011	1.239					│ │ <del>│ <mark>│ </mark>Ⅰ∎ ∏──</del> │ │
	Restrepo, 2002	0.500					<u>↓ ↓ ↓ ↓ ↓ </u>
	Slater, 2009	1.498					│ │ │ ∔∎┼ │ │
	Suksompong, 2002	3.750		12.141			
		1.914		2.530			
							0.1 0.2 0.5 1 2 5 10
	1						

Sex (male)	Study name		Statis	tics for e	ach study		Odds ratio and 95% CI
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
	Baba, 2007	0.972	0.459	2.060	-0.074	0.941	
	Boodhwani, 2006	1.206			0.660	0.509	
	Christiansen, 2016	1.667		58.281	0.282	0.778	
	Colak, 2015	1.322			0.772	0.440	
	deTournay-Jette, 2011				-0.665	0.506	
	Dong, 2014 Goto, 2000	0.811			-0.437 0.548	0.662	
	Hall, 1999	0.574				0.384	
	Harmon, 2005	0.750			-0.305	0.760	
	Kadoi, 2005	0.896			-0.292	0.770	
	Kadoi, 2011b	0.786	0.299	2.061	-0.490	0.624	
	Kumpaitiene, 2019	1.488		4.393	0.719	0.472	
	Mu, 2013	0.988			-0.027	0.979	
	Norkiene, 2011	1.270			0.522	0.602	
	Reents, 2002	1.037			0.039	0.969	
	Restrepo, 2002 Slater, 2009	3.267		82.036	0.720	0.472	
	Suksompong, 2002	0.913			-0.025	0.874	
	s aloonipolig, 2002	1.026			0.223	0.824	
							0.1 0.2 0.5 1 2 5 10
Kidney injury	Ctubi name		Ctatist				Odda ratio and 05% Cl
Xidiley injury	Study name	Odds	Lower	Upper	ach study		Odds ratio and 95% Cl
		ratio	limit	limit	Z-Value	p-Value	
	Baba, 2007	0.860	0.278	2.662	-0.262	0.793	
	Colak, 2015	3.668	0.135	99.509	0.772	0.440	
	Slater, 2009	0.411	0.119	1.416			
	Suksompong, 2002	4.200	1.018		1.985		
	Suksompong, 2002						
		1.213	0.396	3.716	0.338	0.735	
							0.1 0.2 0.5 1 2 5 10
Previous MI <90 days	Study name		Statisti	cs for ea	ch study	ł.	Odds ratio and 95% Cl
Previous MI <90 days		odds	Lower	Upper	ch study		Odds ratio and 95% Cl
Previous MI <90 days	C	Odds I ratio	Lower limit	Upper limit	Z-Value	p-Value	Odds ratio and 95% Cl
Previous MI <90 days	Colak, 2015	Odds I ratio 1.155	Lower limit 0.376	Upper limit 3.552	<b>Z-Value</b> 0.252	<b>p-Value</b> 0.801	Odds ratio and 95% Cl
Previous MI <90 days	Colak, 2015	Odds I ratio	Lower limit	Upper limit	Z-Value	p-Value	Odds ratio and 95% Cl
Previous MI <90 days	Colak, 2015 Norkiene, 2011	Odds I ratio 1.155	Lower limit 0.376	Upper limit 3.552	<b>Z-Value</b> 0.252	<b>p-Value</b> 0.801	Odds ratio and 95% Cl
Previous MI <90 days	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds I ratio 1.155 1.621	Lower limit 0.376 0.528	Upper limit 3.552 4.975	<b>Z-Value</b> 0.252 0.844	<b>p-Value</b> 0.801 0.399	Odds ratio and 95% CI
Previous MI <90 days	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750	Lower limit 0.376 0.528 0.240	Upper limit 3.552 4.975 2.342	<b>Z-Value</b> 0.252 0.844 -0.495	<b>p-Value</b> 0.801 0.399 0.620	Odds ratio and 95% CI
Previous MI <90 days	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750	Lower limit 0.376 0.528 0.240	Upper limit 3.552 4.975 2.342	<b>Z-Value</b> 0.252 0.844 -0.495	<b>p-Value</b> 0.801 0.399 0.620	
Previous MI <90 days Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750	Lower limit 0.376 0.528 0.240 0.586	Upper limit 3.552 4.975 2.342 2.156	<b>Z-Value</b> 0.252 0.844 -0.495	<b>p-Value</b> 0.801 0.399 0.620 0.724	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750 1.124	Lower limit 0.376 0.528 0.240 0.586	Upper limit 3.552 4.975 2.342 2.156 cs for ea	<b>Z-Value</b> 0.252 0.844 -0.495 0.353	<b>p-Value</b> 0.801 0.399 0.620 0.724	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750 1.124 Odds ratio	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit	Z-Value 0.252 0.844 -0.495 0.353 ach study Z-Value	p-Value 0.801 0.399 0.620 0.724	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds 1 ratio 1.155 1.621 0.750 1.124 Odds 1 ratio 1.831	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191	<b>Z-Value</b> 0.252 0.844 -0.495 0.353 <b>ach study</b> <b>Z-Value</b> 1.431	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005	Odds     I       1.155     1.621       0.750     1.124       Odds     I       Ddds     I       1.831     1.246	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977	<b>Z-Value</b> 0.252 0.844 -0.495 0.353 <b>ach study</b> <b>Z-Value</b> 1.431 0.311	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	Odds         I           ratio         1.155           1.621         0.750           1.124         0.750           1.124         0.750           1.124         0.124           Ddds         1.831           1.246         1.776	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015	Z-Value 0.252 0.844 -0.495 0.353 http://doi.org/10.000 ch.study Z-Value 1.431 0.311 2.127	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013	Odds         I           1.155         1.621           0.750         1.124           1.124         1.124           Odds         1.831           1.246         1.776           0.698         1.831	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322	Z-Value 0.252 0.844 -0.495 0.353 http://doi.org/10.000 C-Value 1.431 0.311 2.127 -1.103	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011	Odds         I           1.155         1.621           0.750         1.124           1.124         1.124           Odds         1.831           1.246         1.776           0.698         0.719	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322 1.458	<b>Z-Value</b> 0.252 0.844 -0.495 0.353 <b>ach study</b> <b>Z-Value</b> 1.431 0.311 2.127 -1.103 -0.915	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011 Slater, 2009	Odds         I           1.155         1.621           0.750         1.124           Ddds         I           1.124         I           Ddds         I           1.246         1.776           0.698         0.719           1.345         I	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354 0.590	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322 1.458 3.063	Z-Value 0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127 -1.103 -0.915 0.705	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360 0.481	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011 Slater, 2009 Suksompong, 2002	Ddds         I           1.155         1.621           0.750         1.124           1.124         1.124           Ddds         I           1.831         1.246           1.776         0.698           0.719         1.345           1.030         1.030	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322 1.458	Z-Value 0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127 -1.103 -0.915 0.705 0.054	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360 0.481 0.957	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011 Slater, 2009 Suksompong, 2002	Odds         I           1.155         1.621           0.750         1.124           Ddds         I           1.124         I           Ddds         I           1.246         1.776           0.698         0.719           1.345         I	Lower limit 0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354 0.590	Upper limit 3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322 1.458 3.063	Z-Value 0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127 -1.103 -0.915 0.705	p-Value 0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360 0.481	

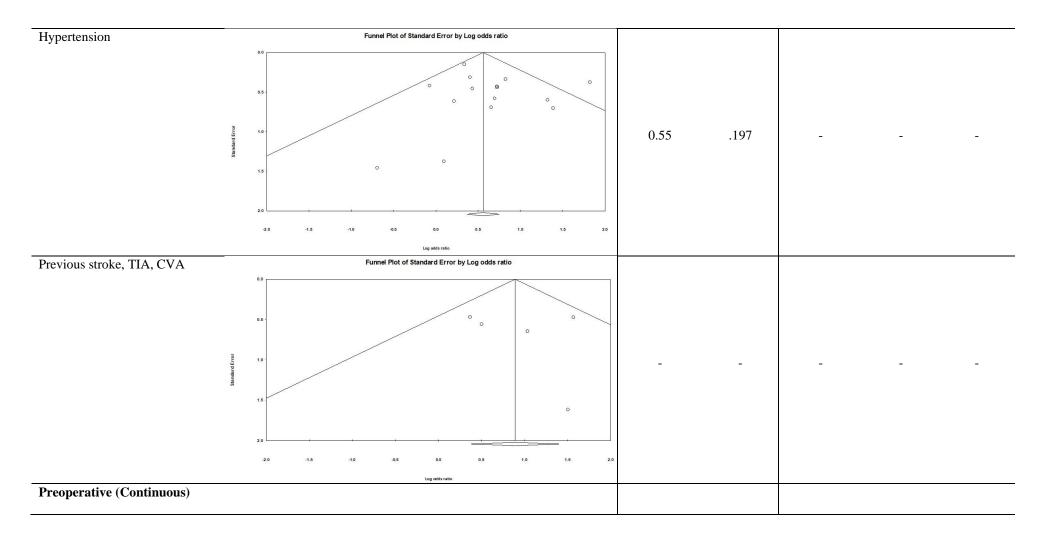
Previous stroke, TIA, CVA	Study name		Statist	ics for ea	ch study	!	Odds ratio and 95% Cl
		Odds ratio	Lower limit		Z-Value	p-Value	
	Baba, 2007	4.799	1.899	12.129	3.315	0.001	
		2.814	0.795	9.959	1.604	0.109	
		1.445	0.576	3.623	0.785	0.433	
	Restrepo, 2002	4.500	0.190	106.823	0.931	0.352	
		1.652	0.553	4.938	0.899	0.369	│ │ │-┼╋┼┤ │
		2.435	1.468	4.038	3.447	0.001	
							0.1 0.2 0.5 1 2 5 10
PVD	Chidu nama		Ctatia	tion for a	ach atud		Odda ratio and 05% Cl
	Study name		30		ach stud	Y	Odds ratio and 95% CI
		Odds ratio		Upper limit	Z-Value	p-Value	
	Baba, 2007	0.414	4 0.12	0 1.432	-1.393	0.164	
	Boodhwani, 2006	0.990	0.56	0 1.748	-0.036	0.971	-#
	Goto, 2000	4.35	3 1.18	5 15.987	2.216	0.027	│ │ │ │ <del>│ → ■</del> →
	Restrepo, 2002	0.48	0.01	8 12.929	-0.431	0.666	<b>           </b>
		1.08	7 0.41	7 2.831	0.170	0.865	
							0.1 0.2 0.5 1 2 5 10
Smoking current/history	Study name		Statis	tics for e	ach study	v	Odds ratio and 95% CI
	10	Odds ratio		Upper		p-Value	
	Baba, 2007	0.902				a second concerns	1 T <b>1 1</b> 1 1 1
	Dong, 2014	1.07					
	Kadoi, 2001	0.100					<u>↓ ↓ ∓ </u> │ │ │
	Kadoi, 2005	1.033		3 1.93			
	Liu, 2009	0.337					
	Mu, 2013	1.382					
	Norkiene, 2011						
	Restrepo, 2002 Slater, 2009	15.000		7 376.696			
	Sidler, 2005	1.03					
							0.1 0.2 0.5 1 2 5 10
Pre-Operative (Continuous)							
Age (years)	Study name	erence Si	Statis	tics for each st			Difference in means and 95% Cl
	in	neans	error Vari	ance limit	Upper limit Z-Value		
	Baba, 2007 Boodhwani, 2006	0.700		0.973 -1.234 0.001 0.425	2.634 0.710 0.575 13.005		
	Christiansen, 2016 Colak, 2015	1.900		0.882 -18.739 1.191 5.161	22.539 0.180 9.439 6.689		
	deTournay-Jette, 2011 Dong, 2014	-3.010		2.368 -6.026	0.006 -1.956		│ ┼╾┤ ▁▁▔│
	Goto, 2000	1.500	1.168	1.384 -0.789	3.789 1.284	0.199	
		3,300	3.234 10	0.460 -3.039 5.883 3.546	9.639 1.020		
	Hall, 1999 Hamon, 2005	8.300					
			1.500	2.251 4.000 1.206 -2.352	9.940 4.060	0.000	│ │ _₄_ ┼┻╌┤
	Hamon, 2005 Kadoi, 2005	8.300 7.000	1.500 1.098 2.176 4	2.251 4.000	9.940 4.000	0.000 0.855 0.066	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiene, 2019 Liu, 2009 Mu, 2013	8.300 7.000 -0.200 4.000 2.000 2.000	1.500 2 1.098 2 2.178 4 1.117 1 1.413 1	2.251 4.000 1.206 -2.352 4.736 -0.265 1.247 -0.188 1.996 -0.769	9.940 4.000 1.952 -0.182 8.265 1.838 4.188 1.791 4.769 1.416	5 0.000 2 0.855 8 0.066 1 0.073 5 0.157	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpatitene, 2019 Liu, 2005 Mu, 2013 Newman, 1987 Norkiene, 2011	8.300 7.000 -0.200 4.000 2.000 2.000 6.800 2.400	1.500 1.098 2.176 1.117 1.413 2.045 1.290	2.251 4.060 1.206 -2.352 4.736 -0.285 1.247 -0.188 1.996 -0.769 4.180 2.793 1.665 -0.129	9.940         4.060           1.952         -0.182           8.285         1.838           4.188         1.791           4.769         1.416           10.807         3.320           4.929         1.860	8 0.000 0.855 8 0.066 1 0.073 9 0.157 5 0.001 0 0.083	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2016 Kumpaitiene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Norkiene, 2011 Reents, 2002 Restrep, 2002	8.300 7.000 4.000 2.000 8.800 2.400 1.000 0.570	1.500 2 1.098 2.176 4 1.117 1.413 2.045 4 1.290 2.465 6 6.428 4	2.251 4.060 1.206 -2.352 4.736 -0.265 1.247 -0.188 1.996 -0.769 4.180 2.793 1.665 -0.129 8.075 -3.831 1.315 -12.028	9.940         4.086           1.952         -0.182           8.285         1.838           4.188         1.791           4.769         1.416           10.807         3.326           4.929         1.886           5.831         0.406           13.168         0.085	5 0.000 2 0.855 8 0.066 0.073 3 0.157 5 0.001 0 0.063 8 0.885 9 0.929	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpatitene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Nordinee, 2011 Reents, 2002	8.300 7.000 -0.200 4.000 2.000 8.800 2.400 1.000	1.500 2 1.098 2.176 4 1.117 1.413 2.045 4 1.290 2.465 6 6.428 4 0.392 6	2.251         4.080           1.206         -2.352           4.736         -0.285           1.247         -0.188           1.996         -0.769           4.180         2.793           1.685         -0.129           3.075         -3.831	9.940 4.050 1.952 -0.182 8.265 1.838 4.188 1.791 4.769 1.416 10.807 3.326 4.929 1.860 5.831 0.406	5 0.000 2 0.855 8 0.066 0.073 8 0.157 5 0.001 0.063 9 0.885 9 0.929 9 0.000	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2016 Kumpaitiene, 2019 Liu, 2005 Mu, 2013 Newman, 1987 Norkiene, 2011 Reents, 2002 Reatrepo, 2002 Stott, 2009 Stater, 2009 Stater, 2009	8.300 7.000 -0.200 4.000 2.000 6.800 2.400 1.000 0.570 5.900 -0.020 2.000	1.500 2 1.098 2 2.176 4 1.117 4 2.045 4 1.290 2 2.485 6 6.428 4 0.392 0 1.313 1.810 2	2.251         4.080           1.206         -2.352           4.736         -0.285           1.247         -0.188           1.996         -0.789           1.685         -0.129           9.075         -3.831           1.315         5.132           9.153         5.132           9.276         -1.548	9.940         4.050           1.952         -0.182           8.265         1.833           4.188         1.791           4.769         1.416           10.807         3.320           4.929         1.860           5.831         0.406           13.168         0.668           5.653         -0.015           5.648         1.105	5         0.000           2         0.855           3         0.066           3         0.157           5         0.001           0         0.063           0         0.855           0         0.063           0         0.929           5         0.988           5         0.269	
	Harmon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpatiene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Norkiene, 2011 Reente, 2002 Restrepo, 2002 Scott, 2002 Slater, 2009	8.300 7.000 -0.200 4.000 2.000 8.800 2.400 1.000 0.570 5.900 -0.020	1.500 2 1.098 2 2.176 4 1.117 1 2.045 4 1.290 2 2.465 4 6.428 4 0.392 4 1.313 1 1.810 2 2.776 7	2.251 4.080 1.206 -2.352 4.736 -0.285 1.247 -0.188 1.996 -0.769 4.180 2.793 1.685 -0.129 9.075 -3.831 1.315 -12.028 0.153 5.132 1.724 -2.593	9.940         4.086           1.952         -0.182           8.265         1.838           4.188         1.791           4.789         1.416           10.807         3.326           4.929         1.860           5.831         0.400           13.168         0.088           2.553         -0.015	0.000           0.855           0.008           0.073           0.157           0.085           0.003           0.083           0.865           0.929           0.0929           0.0988           0.209           0.313           0.000	

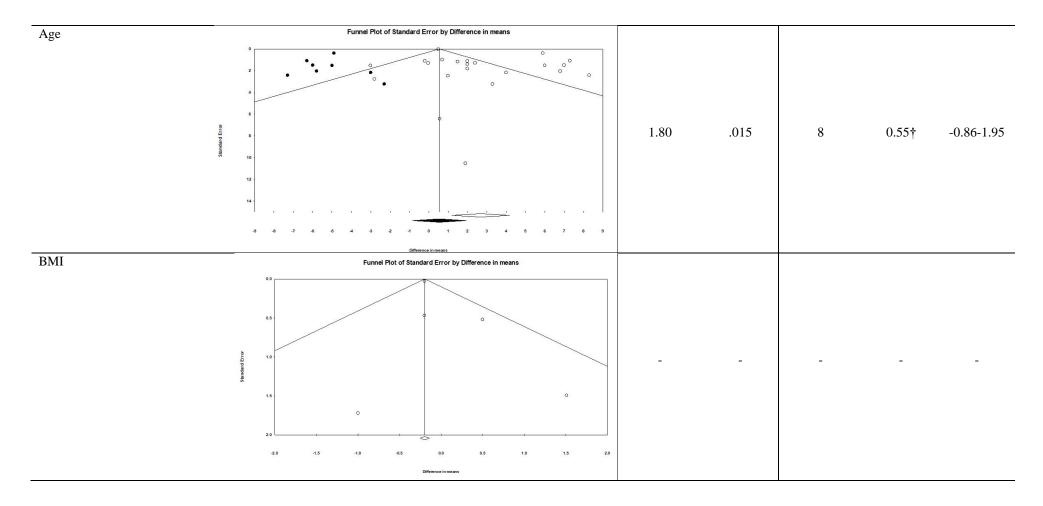
	Study name		-	Statistics for	oreach st	tudy				Difference	e in means a	nd 95% CI	
		Difference in means	Standard	Variance	Lower	Upper limit	Z-Value	p-Value					
	Boodhwani, 2006	-0.200	0.029	0.001	-0.257	-0.143	-6.936	0.000	T.	E.	- 1 C	12	Т
	deTournay-Jette, 2011	1.510		2.234	-1.420	4.440	1.010	0.312		-	08-51		
	Dong, 2014	0.500		0.271	-0.521	1.521	0.960	0.337			_	_	1
	Mu, 2013	-0.200	0.470	0.220	-1.120	0.720	-0.426	0.670		-		-85	
	Norkiene, 2011	-1.000	1.721	2.963	-4.374	2.374	-0.581	0.561	K-		11		-
		-0.197	0.029	0.001	-0.254	-0.141	-6.874	0.000		k,	•	1	1
									-2.00	-1.00	0.00	1.00	2.00
Cognition: All tests	Study name		1	Statistics f	oreach st	tudy				Std diff	in means a	nd 95% CI	
		Std diff in means	Standard	Variance	Lower	Upper limit	Z-Value	n-Value					
	doTouromy latta 2011						2.390	0.017	1	1	1		. 1
	deTournay-Jette, 2011	0.823	0.344	0.119	0.148	1.498	0.685					1.0	- I
	Hall, 1999	0.237	0.346	0.120	-0.441	0.916	-1.086	0.493					
	Kumpaitiene, 2019	0.230	0.334	0.075	-0.425	0.236	0.687	0.492		1.0			
		0.230	0.334	0.112	-0.420	0.004	0.007	0.432	1	10			
									-2.00	-1.00	0.00	1.00	2.00
Cognition: MMSE only	Study name		1	Statistics fo	oreach st	tudy				Difference	e in means	and 95% Cl	5
- *		Difference	Standard	Variante	Lower	Upper	7 Mature	n Matur					
		in means	error	Variance	limit	limit		p-Value	T	1	1.5		1
	deTournay-Jette, 2011	1.110	0.453	0.205	0.223	1.997	2.452	0.014		1000			
	Kumpaitiene, 2019	-0.600	0.550	0.302	-1.677	0.477	-1.092	0.275		-			
		0.283	0.855	0.730	-1.391	1.958	0.332	0.740	1	1 -			1
									-4.00	-2.00	0.00	2.00	4.00
Depression: All tests	Study name		Static	tion for a	ah atud	2				Ctd diff in			
Depression. An tests	Study name	diff Stand	-21 X X X X X X X X X X X X X X X X X X X	tics for ea	wer Up	10.0				Sta airr in	means and	1 95% CI	
		neans err					Value p	Value					
	Harmon, 2004	0.310 0	0.340 (	0.116 -0	976 0	.357 -	0.910	0.363	1	1 -		- I	- 1
	Harmon, 2005	0.039 0	0.342 (	0.117 -0.	709 0	.632 -	0.113	0.910			_		
	Kadoi, 2011b	2.024 0	0.259 (	0.067 1	516 2	532	7.807	0.000			100	-	
	Silbert, 2006	0.274 0	0.151 (	0.023 -0	023 0	.571	1.807	0.071					
		0.501 0	0.499 (	0.249 -0	478 1	.479	1.003	0.316			-	<b>-</b>	
									-4.00	-2.00	0.00	2.00	4.00
									-4.00	-2.00	0.00	2.00	4.00
Education (years)	Study name		1	Statistics f	oreach st	tudy				Differen	ce in means	and 95% CI	
Education (years)	Study name_	Difference	Standard		Lower	Upper				Differen	ce in means	and 95% CI	
Education (years)		in means	Standard error	Variance	Lower limit	Upper limit		p-Value	1	Differen	ce in means	and 95% CI	
Education (years)	Colak, 2015	in means -1.200	Standard error 0.492	Variance 0.242	Lower limit -2.164	Upper limit -0.236	-2.440	0.015	I	<u>Differen</u>	ce in means	and 95% CI	
Education (years)	Colak, 2015 deTournay-Jette, 2011	in means -1.200 1.070	Standard error 0.492 1.436	Variance 0.242 2.063	Lower limit -2.164 -1.745	Upper limit -0.236 3.885	-2.440 0.745	0.015 0.456	1		ce in means	and 95% CI	
Education (years)	Colak, 2015 deTournay-Jette, 2011 Hall, 1999	in means -1.200 1.070 -1.600	Standard error 0.492 1.436 0.913	Variance 0.242 2.063 0.834	Lower limit -2.164 -1.745 -3.390	Upper limit -0.236 3.885 0.190	-2.440 0.745 -1.752	0.015 0.456 0.080			ce in means	and 95% CI	
Education (years)	Colak, 2015 deTournay-Jette, 2011	in means -1.200 1.070	Standard error 0.492 1.436	Variance 0.242 2.063	Lower limit -2.164 -1.745	Upper limit -0.236 3.885 0.190 1.084	-2.440 0.745 -1.752 -1.069	0.015 0.456 0.080	-		ce in means	and 95% Cl	
Education (years)	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005	in means -1.200 1.070 -1.600 -1.300	Standard error 0.492 1.436 0.913 1.217	Variance 0.242 2.063 0.834 1.480	Lower limit -2.164 -1.745 -3.390 -3.684	Upper limit -0.236 3.885 0.190 1.084 3.101	-2.440 0.745 -1.752 -1.069 0.377	0.015 0.456 0.080 0.285	-			and 95% Cl	
Education (years)	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019	in means -1.200 1.070 -1.600 -1.300 0.500	Standard error 0.492 1.436 0.913 1.217 1.327	Variance 0.242 2.063 0.834 1.480 1.761	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646	-2.440 0.745 -1.752 -1.069 0.377	0.015 0.456 0.080 0.285 0.706 0.261	-			and 95% Cl	_
Education (years)	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019	in means -1.200 1.070 -1.600 -1.300 0.500 0.600	Standard error 0.492 1.436 0.913 1.217 1.327 0.534	Variance 0.242 2.063 0.834 1.480 1.761 0.285	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646	-2.440 0.745 -1.752 -1.069 0.377 1.125	0.015 0.456 0.080 0.285 0.706 0.261	-4.00	Differen	ce in means	and 95% Cl	- 4.0
	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019	in means -1.200 1.070 -1.600 -1.300 0.500 0.600	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	Variance 0.242 2.063 0.834 1.480 1.761 0.285	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	-2.440 0.745 -1.752 -1.069 0.377 1.125	0.015 0.456 0.080 0.285 0.706 0.261	-4.00	-2.00		- - 200	- 4.0
	Colak, 2015 deTournay-Jette, 2011 Hal, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013	in means -1.200 1.070 -1.600 -1.300 0.500 0.600 -0.435	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	Variance 0.242 2.063 0.834 1.460 1.761 0.285 0.243	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	-2.440 0.745 -1.752 -1.069 0.377 1.125	0.015 0.456 0.080 0.285 0.706 0.261	-4.00	-2.00	0.00	- - 200	- 4.0
	Colak, 2015 deTournay-Jette, 2011 Hal, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 <u>Study name</u> Diff	in means -1.200 1.070 -1.600 -1.300 0.500 0.600 -0.435 erence Sta	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493 <u>Stat</u> ndard	Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243 0.243	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	-2.440 0.745 -1.752 -1.069 0.377 1.125	0.015 0.456 0.080 0.285 0.706 0.261 0.377	-4.00	-2.00	0.00	- - 200	-
	Colak, 2015 deTournay-Jette, 2011 Hal, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 <u>Study name</u> Diff	in means -1.200 1.070 -1.600 -1.300 0.500 0.600 -0.435 erence Sta	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493 <u>Stat</u> ndard	Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243 0.243	Lower Jimit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stud ower U Jimit	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	-2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883	0.015 0.456 0.080 0.285 0.706 0.261 0.377	-4.00	-2.00	0.00	- - 200	- 4.0
	Colak, 2015 de Tournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019 Mu, 2013 <u>Study name</u> Diff	in means -1.200 1.070 -1.600 -1.300 0.500 0.600 -0.435 erence Star means e	Standard error           0.492           1.436           0.913           1.217           0.534           0.493	Variance 0.242 2.063 0.834 1.480 1.761 0.243 0.243 istics for r L riance	Lower Jimit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stud ower U Jimit	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531 0.531	-2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 <b>Z-Value</b>	0.015 0.456 0.080 0.285 0.706 0.261 0.377 p-Value	-4.00	-2.00	0.00	- - 200	- 4.0
	Colak, 2015 de Tournay-Jette, 2011 Hal, 1999 Harmon, 2005 Kumpaitiene, 2019 Mu, 2013 Study name Diff in Colak, 2015	in means -1.200 1.070 -1.600 -1.300 0.500 0.600 -0.435 erence Star means e 1.000	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243 istics for e riance 0.060 0.046	Lower Jimit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stud power Ulimit 0.519	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531 Upper limit 1.481	-2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 <b>Z-Value</b> 4.075	0.015 0.456 0.080 0.285 0.706 0.261 0.377 <b>p-Value</b> 0.000	-4.00	-2.00	0.00	- - 200	- 4.0
Education (years)	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatilene, 2019 Mu, 2013 <u>Study name</u> Diff in Colak, 2015 Dong, 2014	in means -1.200 1.070 -1.600 0.500 0.600 -0.435 erence Sta means e 1.000 0.600	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493 Statt error Va 0.245 0.214	Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243 istics for e riance 0.060 0.046	Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stuce bewer Ulimit 0.519 0.181 -0.151	Upper limit -0.236 3.885 0.190 1.084 3.101 1.686 0.531 1.646 0.531 <b>by</b> Ipper limit 1.481 1.019	-2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 <b>Z-Value</b> 4.075 2.806	0.015 0.456 0.080 0.285 0.706 0.261 0.377 <b>p-Value</b> 0.000 0.005	-4.00	-2.00	0.00	- - 200	-
	Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatilene, 2019 Mu, 2013 <u>Study name</u> Diff in Colak, 2015 Dong, 2014 Mu, 2013	in means -1.200 1.070 -1.600 0.500 0.600 -0.435 erence Staa means e 1.000 0.600 0.459	Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	Variance 0.242 2.063 0.834 1.460 1.761 0.285 0.243 istics for e riance 0.060 0.046 0.097	Lower limit -2.164 -1.745 -3.364 -2.101 -0.446 -1.400 2ach stuc ower Uimit 0.519 0.181 -0.151 0.252	Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531 0.531 0.531 0.531 0.531 0.531 1.6466 1.646 1.646 1.6466 1.646 1.6466 1.6466 1.6466 1.646	-2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 <b>Z-Value</b> 4.075 2.806 1.475	0.015 0.456 0.080 0.285 0.706 0.261 0.377 <b>p-Value</b> 0.000 0.005 0.140	-4.00	-2.00	0.00	- - 200	-

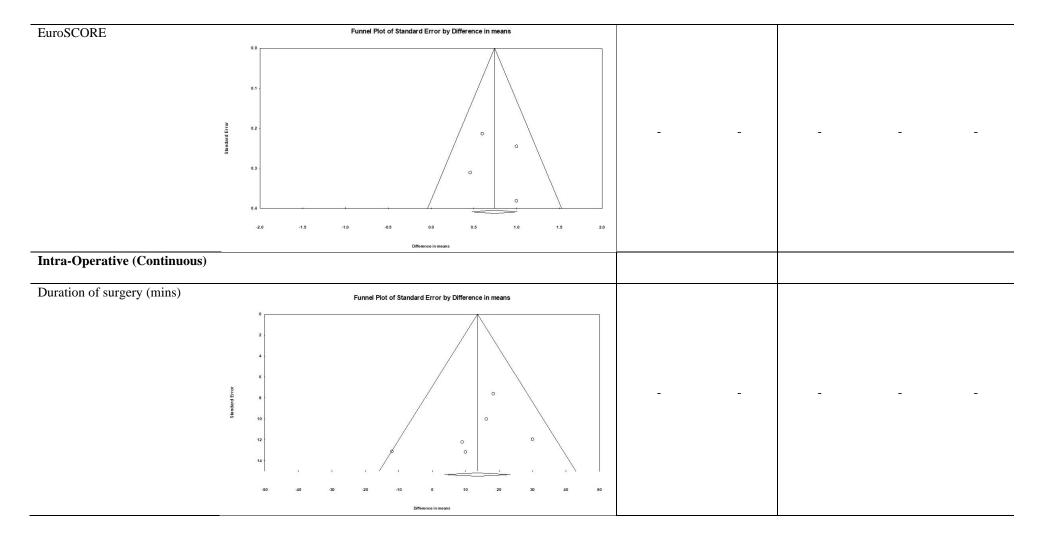
LVEF %	Study name			Statistics for	r each st	udy				Difference	e in means :	and 95% CI	
2.22	22 - 32 - 22	Difference	Standard		Lower	Upper							
		in means	error	Variance	limit	limit	Z-Value	p-Value					
	Harmon, 2005	-9.000	2.336	5.459	-13.579	-4.421	-3.852	0.000	K				- 1
	Kadoi, 2011b	-2.000	1,585	2511	-5.106	1.106	-1.262	0.207	Č.	- 1		-	
	Kadol, 2005 Mu, 2013	-3.000	1.775	3.150 2.829	-6.479	0.479 6.196	-1.690 1.724	0.091	-		-		
	Norkiene, 2011	-2.000	1.462	2.023	-4.865	0.865	-1.368	0.171	(	_			
	Reents, 2002	-10.000	3.109	9.665	-16.093	-3.907	-3.217	0.001	k	T			
	Kumpaitiene, 2019	1.000	2.193	4.810	-3.298	5.298	0.456	0.648		_			,
	Colak, 2015	0.100	1.458	2.125	-2.757	2.957	0.069	0.945		-	-	-	
	Slater, 2009	0.100	1.551	2.406	-2.940	3.140	0.064	0.949		-	-		-
		-1.966	1.147	1.315	-4.213	0.281	-1.715	0.086	k				
									-4.00	-2.00	0.00	2.00	4.00
Intra-Operative (Continuous)													
ACC time (mins)	Study name		100.000 0000000000000000000000000000000	Statistics fo	SHERE WATER	1228 march				Difference	e in means a	nd 95% CI	
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
	Dong, 2014	-4.000	3.672	13.485	-11.197	3.197	-1.089	0.276	k	1	i i	- 1	1
	Hall, 1999	-18.000	5.889	34.679	-29.542	-6.458	-3.057	0.002	È.				
	Jonsson, 2004	-6.500	7.258	52.681	-20.726	7.726	-0.896	0.370	×	-		0	0
	Norkiene, 2010	4.000	2.682	7.195	-1.257	9.257	1.491	0.136			_		
	Restrepo, 2002	2.000	3.657	13.374	-5.168	9.168	0.547	0.584				-	
	Robson, 2000	-2.000	6.786	46.052	-15.301	11.301	-0.295	0.768	<del>&lt;</del>				
	Stump, 1996	2.700	1.814	3.290	-0.855	6.255	1.489	0.137		( good them			
		-1.337	2.333	5.441	-5.909	3.234	-0.573	0.566	J			- 1	
									-10.00	-5.00	0.00	5.00	10.00
CPB time (mins)	Study name			Statistics	for each	etuch				Differenc	e in means	and 95% CI	
	Judy name	Difference	Standard		Lower					Direfelie	c in nicars		
		in means		Variance		limit	Z-Value	p-Value					
	Boodhwani, 2006	-0.10	0.15	6 0.024	4 -0.400	6 0.200	-0.641	0.521	1	- Î		1	Ĩ
	Colak, 2015	7.00										-	28
	Goto, 2000	-6.10										2.23	
	Harmon, 2005 Kadoi, 2005	9.40										_	
	Kadoi, 2005	-3.20						0.408					
	Kumpaitiene, 2019									0	-		
	Newman, 1987	18.60									27	0.2	
	Norkiene, 2011 Reents, 2002	6.00							2		1.000	-	- C
	Slater, 2002	-6.00							5 N 8				
	Smith, 1986	13.00											
	Sylivris, 1998	30.00	0 11.84	6 140.31	6.783	53.21	7 2.533						>
		3.39	0 1.77	8 3.162	2 -0.09	6.87	5 1.907	0.057					1
									-20.00	-10.00	0.00	10.00	20.0
Duration of surgery (mins)	Study mms		6	Statistics for	o sob etu	du				Difformaco	in means an	4 95% CI	
Duration of surgery (mms)	Study name	Difference	- Standard	Statistics fo		upper				Difference	in means an	d 95% CI	
			error	Variance			-Value p-	Value		100		10	21
		in means				22949	0 727	0.461	1	12	-		
	Baba, 2007	9.000	12.219	149.307	-14.949	2.010	0.737	0.401					
	Baba, 2007 deTournay-Jette, 201	9.000	12.219 13.167	149.307 173.366		35.807		0.448				1.000	
	deTournay-Jette, 201 Dong, 2014	9.000 1 10.000 30.000	13.167 11.954	173.366 142.898	-15.807	35.807 53.429	0.759 2.510	0.448 0.012					
	deTournay-Jette, 201 Dong, 2014 Mu, 2013	9.000 1 10.000 30.000 16.200	13.167 11.954 10.029	173.366 142.898 100.584	-15.807 6.571 -3.457	35.807 53.429 35.857	0.759 2.510 1.615	0.448 0.012 0.106		( <u>, n</u>	-		
	de Tournay-Jette, 201 Dong, 2014 Mu, 2013 Norkien e, 2011	9.000 1 10.000 30.000 18.200 18.300	13.167 11.954 10.029 7.616	173.366 142.898 100.584 58.003	-15.807 6.571 -3.457 3.373	35.807 53.429 35.857 33.227	0.759 2.510 1.615 2.403	0.448 0.012 0.106 0.016		_	-		
	deTournay-Jette, 201 Dong, 2014 Mu, 2013	9.000 1 10.000 30.000 18.200 18.300 -12.000	13.167 11.954 10.029 7.616 13.111	173.386 142.898 100.584 58.003 171.891	-15.807 6.571 -3.457 3.373 -37.697	35.807 53.429 35.857 33.227 13.697	0.759 2.510 1.615 2.403 -0.915	0.448 0.012 0.106 0.016 0.360	<				
	de Tournay-Jette, 201 Dong, 2014 Mu, 2013 Norkien e, 2011	9.000 1 10.000 30.000 18.200 18.300	13.167 11.954 10.029 7.616	173.386 142.898 100.584 58.003 171.891	-15.807 6.571 -3.457 3.373	35.807 53.429 35.857 33.227 13.697	0.759 2.510 1.615 2.403 -0.915	0.448 0.012 0.106 0.016 0.360 0.007	<b></b>		-		
	de Tournay-Jette, 201 Dong, 2014 Mu, 2013 Norkien e, 2011	9.000 1 10.000 30.000 18.200 18.300 -12.000	13.167 11.954 10.029 7.616 13.111	173.386 142.898 100.584 58.003 171.891	-15.807 6.571 -3.457 3.373 -37.697	35.807 53.429 35.857 33.227 13.697	0.759 2.510 1.615 2.403 -0.915	0.448 0.012 0.106 0.016 0.360 0.007	30.00	-15.00	0.00	15.00	- 30.0
Intubation time (hours)	de Tournay-Jette, 201 Dong, 2014 Mu, 2013 Norkien e, 2011	9.000 1 10.000 30.000 18.200 18.300 -12.000	13.187 11.954 10.029 7.818 13.111 5.027	173.386 142.898 100.584 58.003 171.891	-15.807 : 6.571 : -3.457 : 3.373 : 3.373 : -37.697 : 3.673 :	35.807 53.429 35.857 33.227 13.697 23.377	0.759 2.510 1.615 2.403 -0.915	0.448 0.012 0.106 0.016 0.360 0.007	30.00		0.00		30.0
Intubation time (hours)	deTournay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002	9.000 1 10.000 30.000 18.200 18.300 -12.000 13.525 Difference	13.167 11.954 10.029 7.816 13.111 5.027 Standard	173.386 142.898 100.584 58.003 171.891 25.266 Statistics fo	-15.807 3 6.571 4 -3.457 3 3.373 3 -37.697 3 3.873 3 50 reach st Lower	35.807 53.429 35.857 33.227 13.697 23.377 <b>udy</b> Upper	0.759 2.510 1.815 2.403 -0.915 2.691	0.448 0.012 0.106 0.016 0.360 0.007	30.00				30.0
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u>	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means	13.167 11.954 10.029 7.616 13.111 5.027 Standard error	173.386 142.898 100.584 58.003 171.891 25.266 Statistics fr Variance	-15.807 3 6.571 4 -3.457 3 3.373 3 -37.697 3 3.673 3 <b>or each st</b> <b>Lower</b> limit	35.807 53.429 35.857 33.227 13.697 23.377 23.377 <b>udy</b> Upper limit	0.759 2.510 1.815 2.403 -0.915 2.691 <b>Z-Value</b>	0.448 0.012 0.106 0.016 0.360 0.007	30.00				30.0
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u> Boodhwani, 2006	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means 2.300	13.167 11.954 10.029 7.616 13.111 5.027 Standard error 0.064	173.386 142.898 100.584 58.003 171.891 25.266 Statistics fr Variance 0.004	-15.807 3 6.571 4 -3.457 3 3.373 3 -37.697 3 3.873 3 50 reach st Lower	35.807 53.429 35.857 33.227 13.697 23.377 23.377 udy Upper limit 2.426	0.759 2.510 1.815 2.403 -0.915 2.691	0.448 0.012 0.106 0.016 0.360 0.007	30.00				30.0
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u>	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means	13.167 11.954 10.029 7.616 13.111 5.027 Standard error	173.386 142.898 100.584 58.003 171.891 25.266 Statistics fr Variance	-15.807 : 6.571 : -3.457 : 3.373 : -37.697 : 3.873 : <b>br each st</b> <b>Lower</b> limit 2.174	35.807 53.429 35.857 33.227 13.697 23.377 23.377 <b>udy</b> Upper limit	0.759 2.510 1.815 2.403 -0.915 2.691 <b>Z-Value</b> 35.907	0.448 0.012 0.106 0.016 0.360 0.007 <b>p-Value</b> 0.000	30.00				30.0
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u> Boodh wani, 2006 Colak, 2015	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means 2.300 1.800	13.167 11.954 10.029 7.816 13.111 5.027 <b>Standard</b> error 0.064 0.581	173.386 142.898 100.584 58.003 171.891 25.266 Statistics fr Variance 0.004 0.337	-15.807 : 6.571 : -3.457 : 3.373 : -37.897 : 3.873 : <b>br each st</b> <b>Lower</b> limit 2.174 : 0.661 :	35.807 53.429 35.857 33.227 13.697 23.377 23.377 <b>udy</b> Upper limit 2.426 2.939	0.759 2.510 1.815 2.403 -0.915 2.691 <b>Z-Value</b> 35.907 3.099	0.448 0.012 0.106 0.016 0.360 0.007 <b>p-Value</b> 0.000 0.002	30.00				30.0
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u> Boodh wani, 2006 Colak, 2015 Liu, 2009	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means 2.300 1.800	13.167 11.954 10.029 7.616 13.111 5.027 <b>Standard</b> error 0.064 0.581 0.784	173.366 142.898 100.584 58.003 171.891 25.266 <b>Statistics fr</b> <b>Variance</b> 0.004 0.337 0.614	-15.807 : 6.571 : -3.457 : 3.373 : -37.697 : 3.873 : or each st Lower limit 2.174 0.661 0.264	35.807 53.429 35.857 33.227 13.697 23.377 23.377 <b>udy</b> <b>Upper</b> <b>limit</b> 2.426 2.939 3.336	0.759 2.510 1.815 2.403 -0.915 2.891 <b>Z-Value</b> 35.907 3.099 2.297	0.448 0.012 0.108 0.018 0.380 0.007 <b>p-Value</b> 0.000 0.002 0.002	30.00				30.0 -
Intubation time (hours)	deToumay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u> Boodhwani, 2006 Colak, 2015 Liu, 2009 Mu, 2013	9.000 1 10.000 30.000 18.200 18.300 -12.000 13.525 Difference in means 2.300 1.800 0.224	13.167 11.954 10.029 7.618 13.111 5.027 Standard error 0.064 0.581 0.784 0.854	173.366 142.898 100.584 56.003 171.891 25.266 <b>Statistics fr</b> <b>Variance</b> 0.004 0.337 0.614 0.729	-15.807 : 6.571 : -3.457 : 3.373 : -37.697 : 3.673 : or each st Lower limit 2.174 : 0.661 : 0.264 -1.449 : -1.449 : -1.580 : -1.580 : -3.580 : -3.457	35.807 53.429 35.857 33.227 13.697 23.377 <b>udy</b> <b>Upper</b> <b>limit</b> 2.426 2.939 3.336 1.898	0.759 2.510 1.815 2.403 -0.915 2.891 <b>Z-Value</b> 35.907 3.099 2.297 0.263	0.448 0.012 0.106 0.016 0.360 0.007 <b>p-Value</b> 0.000 0.002 0.022 0.793	30.00				30.0
Intubation time (hours)	deTournay-Jette, 201 Dong, 2014 Mu, 2013 Norkiene, 2011 Reents, 2002 <u>Study name</u> Boodhwani, 2006 Colak, 2015 Liu, 2009 Mu, 2013 Norkiene, 2011	9.000 1 10.000 30.000 16.200 18.300 -12.000 13.525 Difference in means 2.300 1.800 0.224 2.082	13.167 11.954 10.029 7.616 13.111 5.027 Standard error 0.064 0.581 0.784 0.854 1.511	173.366 142.898 100.584 58.003 171.891 25.266 <b>Statistics fr</b> <b>Variance</b> 0.004 0.337 0.614 0.729 2.282	-15.807 : 6.571 : -3.457 : 3.373 : -3.7897 : 3.873 : <b>br each st</b> <b>cower</b> <b>limit</b> 2.174 0.661 0.264 -1.449 -0.879	35.807 53.429 35.857 33.227 13.897 23.377 23.377 <b>udy</b> <b>Upper</b> <b>limit</b> 2.426 2.939 3.336 1.898 5.043	0.759 2.510 1.815 2.403 -0.915 2.691 <b>Z-Value</b> 35.907 3.099 2.297 0.263 1.378	0.448 0.012 0.106 0.018 0.380 0.007 <b>p-Value</b> 0.000 0.002 0.022 0.793 0.168	30.00				30.0

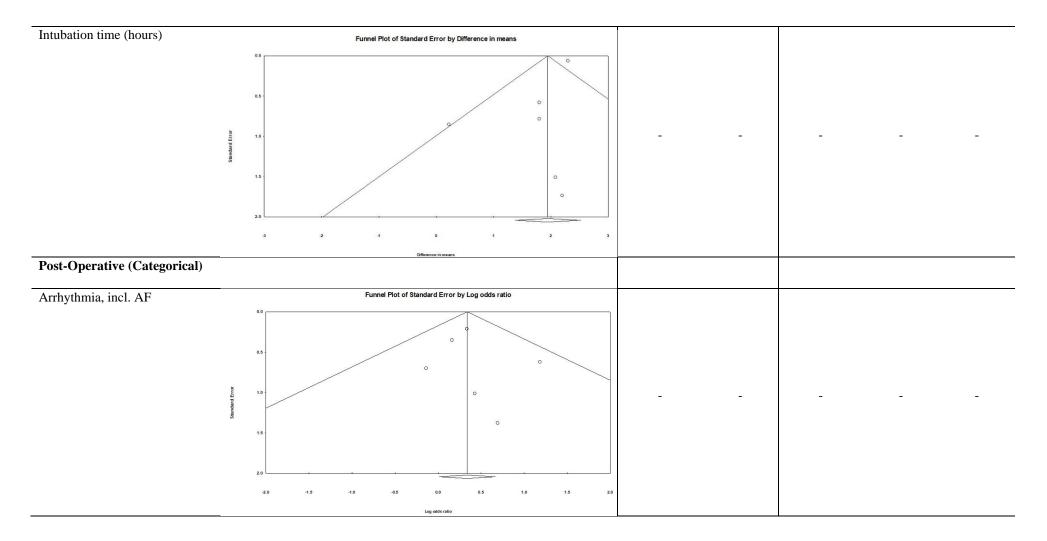
Number of grafts	Study name			Statistic	s for each	study				Di	fferencei	in means	and 95% Cl	
		Difference in means		Varian	Lower ce limit	Upper limit	Z-Value	p-Value						
	Boodh wani, 2006	0.00					0.000	1.000	Ê		Ĕ		Ĩ	Ĩ
	Colak, 2015	0.10					1.100					- <del>T</del> +-	-8	
	Dong, 2014	0.20	0 0.22	6 0.0	51 -0.243	0.643	0.884	0.377			<u>-</u>	-	-	
	Harmon, 2005	0.20					0.461	0.645		532	-	-		$\rightarrow$
	Mu, 2013 Norkiene, 2011	0.20					1.212	0.226						
	Reents, 2002	-0.20					-0.693	0.489					-	
	100113,2002	0.02					0.842	0.400						
									-1.00	. I.	0.50	0.00	0.50	1.0
												0.00	0.00	
Total Microemboli	Study name	Std diff		Statistics	for each s Lower	tudy Upper				S	td diff in I	means ar	nd 95% Cl	
		means		Variance			Value	p-Value						
	Liu, 2009	0.236	0.134	0.018	-0.026	0.499	1.763	0.078			1		<b>-</b>	- 1
	Rodriguez, 2010	-0.055	0.107	0.01	-0.264	0.154	-0.512	0.608			13	-		
	Royse, 2000	0.681	0.550	0.302	2 -0.397	1.758	1.238	0.216					-	)
	Stump, 1996	0.295	0.170	0.029	-0.038	0.627	1.736	0.082						
		0.157	0.113	0.013	3 -0.066	0.379	1.381	0.167						
									-1.00	-(	0.50	0.00	0.50	1.0
Post-Operative (Categorical)														
Arrhythmia, incl. AF	Study name			tatiati	n for o	ah atu				Od	do roti	o ond i	05% CI	
•	Surdy Hame	C			cs for ea		_			Ou	us rau	U anu	95% CI	
		1	ratio I	limit	limit	Z-Value	e p-V	alue						
	Boodhwani, 200	06	1.398	0.922	2.122	1.57	6 0	0.115	1	1	1	+-	+ I	1
	Colak, 2015			0.591	2.342	0.46		0.644			12	-		
														8
	Mu, 2013				11.147	0.42		0.674						7
	Norkiene, 2011		3.265	0.966	11.035	1.90	5 0	0.057				-		)
	Restrepo, 2002	:	2.000	0.134	29.808	0.50	3 (	0.615		-		-	+ +	- >
	Suksompong, 2	002 (	0.870	0.220	3.435	-0.19	9 (	0.842		-	-	-		
	ouroompong, z			1.013	1.941	2.03		0.042						
			1.402	1.015	1.941	2.03	0 0	0.042	1	1	2		1 1	
														10
									0.1	0.2	0.5	1	2 5	
Delirium	Study name		Sta	atistics	s for ea	chstu	dv		0.1					1
Delirium	Study name				s for ea	chstu	ły		0.1				2 5 95% C	!
Delirium	Study name		is Lov		Jpper	ch stud Z-Valu		Value	0.1					ļ
Delirium		Odc rati	is Lov io lin	ver L nit	Jpper limit	Z-Valu	e p-\		0.1					ļ
Delirium	Colak, 2015	Odc rati 4.1	is Lov io lin 71 1.4	ver L nit 458	Jpper limit 11.935	<b>Z-Valu</b> 2.66	e p-\ 2 (	800.0	0.1					, ,
Delirium		Odc rati 4.1	is Lov io lin 71 1.4	ver L nit 458	Jpper limit	Z-Valu	e p-\ 2 (		0.1					!
Delirium	Colak, 2015 Norkiene, 201	Odc rati 4.1 1 9.0	is Lov io lin 71 1 19 1	ver L nit 458 076	Jpper limit 11.935 75.621	<b>Z-Valu</b> 2.66 2.02	e p-\ 2 ( 7 (	0.008 0.043	0.1					!   
Delirium	Colak, 2015	Odc rati 4.1 1 9.0 39.0	<b>is Lov</b> io lin 71 1.4 19 1.4 00 2.4	ver L nit 458 076 021 75	Jpper limit 11.935 75.621 52.636	<b>Z-Valu</b> 2.66 2.02 2.42	e p-\ 2 ( 7 ( 6 (	0.008 0.043 0.015	0.1					-
Delirium	Colak, 2015 Norkiene, 201	Odc rati 4.1 1 9.0	<b>is Lov</b> io lin 71 1.4 19 1.4 00 2.4	ver L nit 458 076 021 75	Jpper limit 11.935 75.621	<b>Z-Valu</b> 2.66 2.02	e p-\ 2 ( 7 ( 6 (	0.008 0.043	0.1					
Delirium	Colak, 2015 Norkiene, 201	Odc rati 4.1 1 9.0 39.0	<b>is Lov</b> io lin 71 1.4 19 1.4 00 2.4	ver L nit 458 076 021 75	Jpper limit 11.935 75.621 52.636	<b>Z-Valu</b> 2.66 2.02 2.42	e p-\ 2 ( 7 ( 6 (	0.008 0.043 0.015				io and		
Delirium Post-Operative (Continuous)	Colak, 2015 Norkiene, 201	Odc rati 4.1 1 9.0 39.0	<b>is Lov</b> io lin 71 1.4 19 1.4 00 2.4	ver L nit 458 076 021 75	Jpper limit 11.935 75.621 52.636	<b>Z-Valu</b> 2.66 2.02 2.42	e p-\ 2 ( 7 ( 6 (	0.008 0.043 0.015		<u>Odd</u>	ls rati	io and	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002	Odc rati 4.1 1 9.0 39.0	<b>is Lov</b> io lin 71 1.4 19 1.4 00 2.4	ver L nit 458 076 021 322	Jpper limit 11.935 75.621 52.636 16.269	<b>Z-Valu</b> 2.66 2.02 2.42 3.65	e p-\ 2 ( 7 ( 6 (	0.008 0.043 0.015		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201	Odc rati 4.1 1 9.0 39.0	ls Lov io lin 71 1 19 1 00 2 47 2	ver L nit 458 076 021 75 322	Jpper limit 11.935 75.621 52.636	<b>Z-Valu</b> 2.66 2.02 2.42 3.65	e p-\ 2 ( 7 ( 6 (	0.008 0.043 0.015 0.000		0dd	ls rati	io and   1	95% C	
	Colak, 2015 Norkiene, 201 Reents, 2002	Oddc rati 4.1 1 9.0 39.0 6.1	Is         Lov           io         lin           71         1.4           19         1.4           00         2.4           47         2.4	ver L nit 458 076 322 322 <u>Statisti</u> rd Varia	Upper limit           11.935           75.621           52.636           16.269           cs for each           cs for each           Lowence           Lowence	<b>Z-Valu</b> 2.66 2.02 2.42 3.65 study	e p-\ 2 () 7 () 6 () 7 () 7 ()	0.008 0.043 0.015 0.000		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 <u>Study name</u> Boodhwani, 2006	Odc rati 4.1 1 9.0 39.0 6.1	Is         Lov           io         lin           71         1.4           19         1.4           00         2.4           47         2.4           ce         Standard           rs         error           290         0.0	ver L nit 458 076 021 322 <u>Statisti</u> rd Varia	Jpper limit 11.935 75.621 52.636 16.269 	<b>Z-Valu</b> 2.66 2.02 2.42 3.65 study Upper limit 4 0.306	e p-\ 2 () 7 () 6 () 7 () 7 () 7 () 7 () 7 () 7 () 7 () 7	0.008 0.043 0.015 0.000		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 <u>Study name</u> Boodhwani, 2006 Colak, 2015	Odc rati 4.1 1 9.0 39.0 6.1 Different in mean 0:: 0::	Is         Lov           io         lin           71         1.4           19         1.4           00         2.4           47         2.4           ce         Standan           reror         error           290         0.0           300         0.1	ver L nit 458 076 021 75 322 <u>Statisti</u> rd Varia 108 0 46 0	Upper limit 11.935 75.621 52.636 16.269 (16.269)	Z-Valu 2.66 2.02 2.42 3.65	e p-\ 2 (( 7 () 6 () 7 () 7 () 7 () 7 () 7 () 7 () 7 () 7	0.008 0.043 0.015 0.000 p-Value 0.000 0.039		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 <u>Study name</u> Boodhwani, 2006 Colak, 2015 deTournay-Jette, 2011	Odc rati 4.1 1 9.0 39.0 6.1 Differen in mean 0.: 0.: 0.: 0.: 0.: 0.: 0.:	Is         Lov           io         lin           71         1.4           19         1.1           00         2.1           47         2.3           ens         series           series         standar           250         0.0           300         0.1           710         0.4	ver L nit 458 076 021 7 322 322 <u>Statisti</u> rd Varia 08 0 46 0 46 0 79 0	Jpper limit 11.935 75.621 52.636 16.269 16.269	Z-Valu 2.66 2.02 2.42 3.65 study Upper limit 4 0.306 5 0.585 9 0.229	e p-1 2 ( 7 ( 6 ( 7	0.008 0.043 0.015 0.000 .000 0.000 0.039 0.138		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 <u>Study name</u> Boodhwani, 2006 Colak, 2015	Oddc rati 4.1 1 9.0 39.0 6.1 Different in mean 0.2 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1 0.1	Is         Lov           io         lin           71         1.4           19         1.1           00         2.1           47         2.3           47         2.3           290         0.0           300         0.1           710         0.4	ver L nit 458 076 322 322 <u>Statisti</u> rd Varia 108 0 46 0 88 0	Jpper limit 11.935 75.621 52.636 16.269 16.269	Z-Valu 2.66 2.02 2.42 3.65 study Upper limit 4 0.585 9 0.229 4 0.444	e p-\ 2 (( 7 () 6 () 7 () 7 () 7 () 7 () 7 () 7 () 7 () 7	0.008 0.043 0.015 0.000 0.000 0.000 0.039 0.138 0.691		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 2011 Harmon, 2005	Odc rati 4.1 1 9.0 39.0 6.1 Differen in mean 0.2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	Is         Lov           io         lin           io         lin           71         1.4           19         1.4           00         2.4           47         2.3           290         0.0           300         0.1           710         0.4           075         0.1           242         0.22           500         0.2	ver L nit 458 076 322 322 <u>Statisti</u> rd Varia 108 0 46 0 46 0 46 0 46 0 46 0 46 0 0 40 0 0	Jpper limit 11.935 75.621 52.636 16.269 16.269	Z-Valu 2.66 2.02 2.42 3.65 ************************************	e p-1 2 ( 7 ( 6 ( 7	0.008 0.043 0.015 0.000 0.000 0.000 0.039 0.138 0.691		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 2011 Harmon, 2005 Mu, 2013	Odc rati 4.1 1 9.0 39.0 6.1 Different in measure in mea	Is         Lov           io         lin           io         lin           71         1.4           19         1.4           19         1.4           00         2.4           47         2.3           290         0.0           300         0.1           710         0.4           075         0.1           242         0.2           200         0.2	ver L nit 458 076 021 75 322 322 <u>Statisti</u> rd Varia 08 0 46 0 46 0 88 0 40 0 16 0 0	Jpper limit 11.935 75.621 52.636 16.269 16.269	Z-Valu 2.66 2.02 2.42 3.65 study Upper limit 4 0.306 5 0.585 9 0.229 4 0.444 2 0.228 4 0.444 2 0.228 4 0.124 0 1.670	e p-1 2 ( 7 ( 6 ( 7 ( 2060 -1.481 -1.010 2.774 5.007	0.008 0.043 0.015 0.000 0.000 0.039 0.138 0.691 0.312 0.006 0.000		0dd	ls rati	io and   1	95% C	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 201 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 2011 Harrion, 2005 Mu, 2013 Norkiene, 2011	Odc rati 4.1 1 9.0 39.0 6.1 Different in measure in mea	Is         Lov           io         lin           io         lin           71         1.4           19         1.4           19         1.4           00         2.4           47         2.3           290         0.0           300         0.1           710         0.4           075         0.1           242         0.2           200         0.2	ver L nit 458 076 322 322 <u>Statisti</u> rd Varia 08 0 46 0 46 0 88 0 46 0 16 0 0 16 0 0	Jpper limit 11.935 75.621 52.636 16.269 16.269	Z-Valu 2.66 2.02 2.42 3.65 * Upper limit 4 0.306 5 0.585 9 0.229 4 0.444 2 0.228 4 0.444 2 0.228 6 1.024 0 1.670	e p-1 2 ( 7 ( 6 ( 7 ( 2060 2060 2060 2060 2060 2060 2060 206	0.008 0.043 0.015 0.000 0.000 0.039 0.691 0.312 0.006		0dd	ls rati	io and   1	95% C	

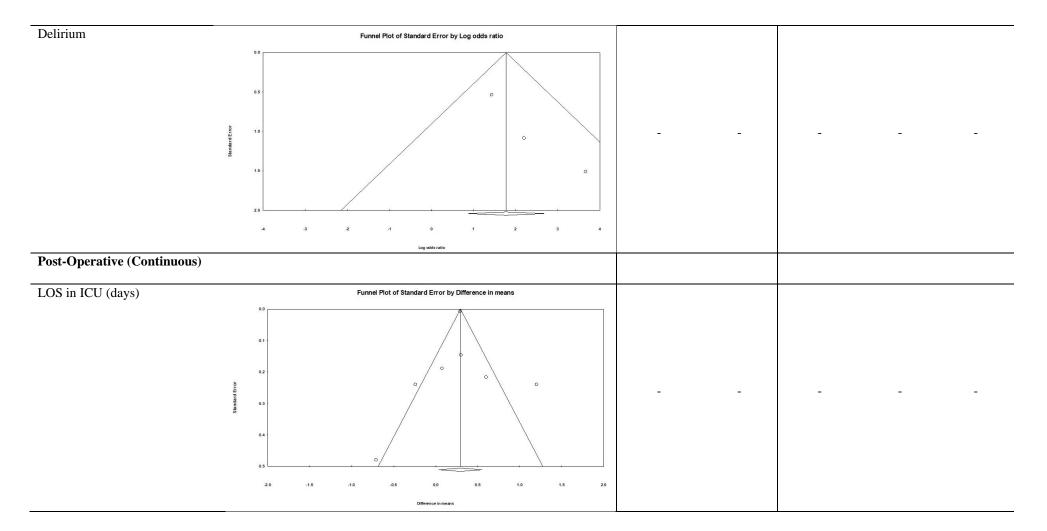
Figure S4. Funne	l plots for statistically significant analyses in regard to acute	Egger'	s Test	ר	<b>Frim and Fill</b>	
-	post-CABG, and results of publication bias/small-study effect en more than 10 studies were available.	Intercept	p value (1-tailed)	No. imputed studies	OR/MD† /SMD‡	95%CI
Preoperative (Catego	orical)					
Depression	Only 2 studies, could not produce funnel plot			-	-	-
Diabetes	Funel Plot of Standard Error by Log odds ratio	-0.39	.232	_	-	-











## Figure S5. Forest plots for mid-term cognitive decline post-CABG analyses.

Variable	Forest Plot														
Pre-Operative (Categorical)															
Depression	Study name_Comp	arison		Statis	tics f	oreach	study			0	)ddsra	tio ar	nd 95%	CI	
			Odds ratio	Lower limit			Value	p-Value							
									Ĩ.	1	1	1	1.1	- 1	1
	Kadoi, 2011b Blank		3.365	1.21		298	2.340	0.019				1			
	Smith, 2000 Blank		2.000	0.82	5 4	851	1.533	0.125				+	-		
			2.504	1.28	4 4	883	2.693	0.007				. 3	-		
									0.1	0.2	0.5	1	2	5	10
Diabetes		~			0						<u></u>		1054 0		
Diabetes	Study name	Comp	arison	Odds L		Alexandrea Latera	ach stud	<u>iy</u>			Odds ra	atio an	nd 95% C	<u>.</u>	
					limit	limit	Z-Value	e p-Value							
	deTournay-Jette, 2011	Blank		0.719	0.237	2.179	-0.58	4 0.560	1	10		-	-	- I	
	Dieleman, 2009	Blank		1.403	0.384	5.131	0.51	2 0.609			-	-+-	-	0	
	Dijk, 2004	Blank		1.096	0.463	2.595	0.20	8 0.835			-				
	Kadoi, 2002	Blank		3.500	0.645	18.980	1.45	2 0.146			3			-	>
	Kadoi, 2005	Blank		3.163	1.562										
	Kadoi, 2007	Blank		6.894	2.511						12.14		-		
	Liu, 2009	Blank		0.375	0.104	1.347					-	$\pm$			
	Mathew, 2006	Blank		1.050	0.366	3.014						-			
	Mathew, 2007	Blank		1.138	0.762	1.701						-			
	Swaminathan, 2002	Blank		1.765	0.975	3.196							-		
				1.536	0.984	2.396	1.89	0 0.059	0.1	0.2	0.5	1	2	5	10
Sex (male)	Study name	Compa	arison	_	Statisti	cs for ea	ach study	<u>y</u>			Odds ra	tio an	d 95% C		
					ower imit	Upper limit	Z-Value	p-Value							
	deTournay-Jette, 2011	Blank		1.556	0.359	6.739	0.591	0.555	Ĩ	-	+	-		+	1
	Dieleman, 2009	Blank		0.679	0.256	1.802	-0.777	7 <u>0.437</u>		8.					
	Dijk, 2004	Blank			0.531	1.884	-0.000				-	+	-		
	Kadoi, 2007	Blank			0.324	2.007	-0.464				-	-			
	Kadoi, 2011b	Blank			0.333	3.283	0.077				-	. 1			
	Kadoi, 2005	Blank			0.318	1.436	-1.018								
	Khatri, 1999 Mathew, 2007	Blank Blank			0.331	1.354	-1.116								
	Mathew, 2007 Mathew, 2006	Blank			0.363	2.757	0.000								
	Smith, 2000	Blank			0.420	1.769	-0.405								
	Swaminathan, 2002	Blank		1000000	0.868	2.558	1.447								
	Slater, 2009	Blank			0.359	2.062	-0.338				+	-			
	Est and				0.818	1.234	0.043			10	8	+			
									0.1	0.2	0.5	1	2	5	10
	1								100	SHE	242	1.20	0.	5	

Hypertension	Study name		Statisti	cs for e	ach study	<u>/</u>	(	Odds ratio and 95% CI
		Odds ratio	Lower limit		Z-Value	n-Value		
	deTournay-Jette, 2011	1.016		3.026	0.028	0.978	1.1	<u> </u>
	Dieleman, 2009	0.901	0.341	2.375		0.833		
	Kadoi, 2001	0.200		0.400		0.000		
	Kadoi, 2002	0.500		1.936		0.316	_	
	Kadoi, 2003	0.300	0.087	1.039	<mark>-1.8</mark> 99	0.058	<	
	Kadoi, 2005	0.925	0.438	1.954	-0.205	0.837		
	Kadoi, 2007	1.195			0.381	0.703		
	Kadoi, 2011b	1.222		3.273	0.399	0.690		
	Mathew, 2006	2.092		6.991	1.200	0.230		
	Mathew, 2007	1.000		1.450		1.000		
	Smith, 2000	1.000		1.722 3.386		1.000 0.003		
	Swaminathan, 2002	0.887				0.558		
		0.007	0.004	1.524	-0.500	0.000	0.1 0.2	2 0.5 1 2 5 10
							0.1 0.4	2 0.5 1 2 5 10
Previous MI history/ever	Study name	Sta	tistics f	or each	n study		00	dds ratio and 95% CI
	Odd		ver Upp nit lin		Value p	-Value		
	Mathew, 2006 0.64				0.904	0.366	11	
	Mathew, 2007 0.72				1.509	0.131		
					0.995			
	Smith, 2000 1.31					0.320		
	0.88	3 0.5	68 1.	373 -	0.553	0.580	1 1	
							0.1 0.2	2 0.5 1 2 5 10
Previous stroke, TIA, CVA	Study name Comparis	on	Statis	tics for e	each study	<u></u>		Odds ratio and 95% CI
		Odd						
	Fato Street, Color	rati	o limit	limit		p-Value		
	Dijk, 2004 Blank	0.7				0.721		
	Mathew, 2007 Blank	0.9						
		0.8	27 0.26	2.628	-0.322	0.748		
							0.1 0.2	0.5 1 2 5 10
PVD								
2	Study name Comparis				each stud	У		Odds ratio and 95% CI
		Od or rat		r Upper limit		p-Value		
	Dijk, 2004 Blank	1.0	00 0.34	7 2.88	5 0.000	1.000	1 1	
	Mathew, 2007 Blank	0.6						
			20 0.00	1.11	3 1,430	0.145		
	Wallew, 2007 Dialik		08 0.41	1 1 21	3 1 2 5 6	0 200		
	Wallew, 2007 Dialik	0.7	08 0.41	4 1.21	3 -1.256	0.209		
	Madiew, 2007 Dialik		08 0.41	4 1.21	3 -1.256	0.209	0.1 0.1	
Smoking (current)		0.7	A 24 25 25 2			0.209	1.424	
Smoking (current)	Study name Odds	0.7 <u>Stat</u>	istics fo	or each		0.209	1.424	2 0.5 1 2 5 1
Smoking (current)	Study name	0.7 <u>Stat</u>	istics fo	or each ber			1.424	
Smoking (current)	<u>Study name</u> Odds	0.7 <u>Stat</u> Lowe	istics fo er Upp t lin	oreach Der Dit Z-V	study		1.424	
Smoking (current)	Study name Odds ratio	0.7 <u>Stat</u> Lowe limi	istics fo er Upp t lin 57 1.4	oreach oer hit <b>Z-</b> 1	<u>istudy</u> Value p	o-Value	1.424	
Smoking (current)	Study name Odds ratio Djaiani, 2003 0.982 Kadoi, 2001 0.900	0.7 <u>Stat</u> Lowe limi 2 0.6 0 0.2	istics fo er Upp t lin 57 1.4 22 3.6	oreach oer hit <b>Z-</b> 1 167 - 556 -	<b>study</b> Value p 0.089 0.147	0.929 0.883	1.424	
Smoking (current)	Study name Odds ratio Djaiani, 2003 0.982 Kadoi, 2001 0.900 Kadoi, 2002 0.700	0.7 <u>Stat</u> Lowe limi 2 0.6 0 0.2 0 0.2	istics for er Upp t lin 57 1.4 22 3.6 11 2.3	er each her hit <b>Z-</b> 167 - 556 - 322 -	<b>study</b> Value p 0.089 0.147 0.583	0.929 0.883 0.560	1.424	
Smoking (current)	Study name           Odds ratio           Djaiani, 2003         0.982           Kadoi, 2001         0.900           Kadoi, 2002         0.700           Kadoi, 2003         0.700	0.7 Stat Lowe 1 0.6 0.2 0.2 0.2 0.2 0.2	istics for er Upp t linn 57 1.4 22 3.6 11 2.3 30 3.7	er each er hit <b>Z-</b> 656 - 622 - 770 -	<b>study</b> Value p 0.089 0.147 0.583 0.415	0.929 0.883 0.560 0.678	1.424	
Smoking (current)	Study name           Odds ratio           Djaiani, 2003         0.982           Kadoi, 2001         0.900           Kadoi, 2002         0.700           Kadoi, 2003         0.700           Kadoi, 2005         1.275	0.7 Stat Lowe 1 0.6 0 0.2 0 0.2 0 0.1 0 0.1 0 0.6	er Upp t lin 57 1.4 22 3.6 11 2.3 30 3.7 55 2.4	er each er hit Z- 656 - 622 - 770 - 145	<b>value p</b> 0.089 0.147 0.583 0.415 0.733	0.929 0.883 0.560 0.678 0.464	1.424	
Smoking (current)	Study name           Odds ratio           Djaiani, 2003         0.982           Kadoi, 2001         0.900           Kadoi, 2002         0.700           Kadoi, 2003         0.700	0.7 Stat Lowe 1 0.6 0 0.2 0 0.2 0 0.1 0 0.1 0 0.6	er Upp t lin 57 1.4 22 3.6 11 2.3 30 3.7 55 2.4	er each er hit Z- 656 - 622 - 770 - 145	<b>study</b> Value p 0.089 0.147 0.583 0.415	0.929 0.883 0.560 0.678	1.424	dds ratio and 95% CI

Age (years)	Study name			tatistics for	each stu	dy				Difference	in means an	d 95% CI	
		Difference	Standard			Upper		22.000					
	100000000000000000000000000000000000000	in means	error	Variance				-Value					
	Braekken, 1998 deTournay-Jette, 2011	7.605	6.935 1.236	48.090 1.529	-5.987 -3.903	21.197 0.943	1.097	0.273 0.231	1 -				-
	Dieleman, 2009	0.200	2.171	4.713	4.055	4.455	0.092	0.927				_	
	Dijk, 2004	0.000	1,320	1.742	-2.587	2.587	0.000	1.000	1		-	- 11	
	Kadol, 2005	1.000	1.775	3.149	-2.478	4.478	0.564	0.573	1	-		-	
	Kadoi, 2007	6.000	2.503	6.267		10.907	2,397	0.017	1			-	-
	Kadol, 2011b Liu, 2009	1.900	1.501	2.253 3.748	-1.042 0.507	4.842	1.266	0.205	1				
	Mathew, 2008	3.000	2.507	6.283	-1.913	7.913	1.197	0.231	1	22	_		
	Mathew, 2007	0.400	0.958	0.914	-1.474	2.274	0.418	0.676	1	26		100	
	Robson, 2000	4.000	2.847	8.103	-1.579	9.579	1.405	0.160	1	<u></u>		-+	-
	Swaminathan, 2002	0.000	1.271	1.615	-2.491	2.491	0.000	1.000	1	-	-		
		1.093	0.589	0.346	-0.060	2.247	1.858	0.063	1				1
									-8.00	-4.00	0.00	4.00	8.00
1													
Cognition: All tests	Study name	C 4 4 1 6 6	Chandrad	Statistics	SZ1000000	- 112 A.				Std diff	in means ar	nd 95% CI	
		Std diff in means	Standard	Variance	Lower	Upper		p-Value					
	deTournay-Jette, 2011	-0.256	0.267			0.266	5 -0.961	0.336	1	1.1	10.0	- 12	- T.
	Mathew, 2007	0.396	0.093							0			
	Swaminathan, 2002	0.483				0.724					52572		
		0.303	0.148	0.022	0.013	0.593	3 2.048	0.041	1				1
									-1.00	-0.50	0.00	0.50	1.00
										_			
Cognition: CI only	Study name	Difference	nan mende	Statistics f	30-0000-0	100				Differenc	ce in means	and 95% CI	
		Difference in means	Standard	Variance	Lower	Upper	Z-Value	p-Value					
	Mathews 2007								1	1	1.	. 1	1
	Mathew, 2007	0.189	0.044	0.002									_
	Swaminathan, 2002	0.880	0.222	0.049	0.445	1.315							
		0.500	0.344	0.118	-0.174	1.174	4 1.455	5 0.146	- L				
									-1.00	-0.50	0.00	0.50	1.00
										-0.00	0.00	0.00	1.01
Depression: All tests	Study name		SI	atistics for	r each st	udv				Std diff i	in means a	nd 95% CI	
Depression: All tests	Study name			atistics for		Contractor and				Std diff i	in means a	nd 95% CI	
Depression: All tests	s		andard	I	Lower	Upper	7.Value	n.Value		Std diff	in means a	nd 95% CI	
Depression: All tests	S	means	andard error <mark>V</mark>	l ariance	Lower limit	Upper limit		p-Value		<u>Std diffi</u>	in means a	nd 95% CI	
Depression: All tests	s		andard	I	Lower	Upper	Z-Value 0.000	<b>p-Value</b> 1.000		<u>Std diff i</u>	in means a	nd 95% CI	Ĩ
Depression: All tests	S in	means	andard error <mark>V</mark>	l ariance	Lower limit	Upper limit				<u>Std diff i</u>	in means a	nd 95% CI	-
Depression: All tests	S in Harmon, 2004	means 0.000	andard error V 0.333	ariance 0.111	Lower limit -0.653	Upper limit 0.653	0.000	1.000		<u>Std</u> diff i	in means a	nd 95% CI	-
Depression: All tests	S in Harmon, 2004 Kadoi, 2011b	means 0.000 2.532 0.060	andard error V 0.333 0.313 0.172	Variance 0.111 0.098 0.029	Lower limit -0.653 1.919 -0.277	Upper limit 0.653 3.144 0.396	0.000 8.098 0.348	1.000 0.000 0.728		<u>Std diff i</u>	in means a	nd 95% CI	-38
Depression: All tests	S in Harmon, 2004 Kadoi, 2011b	means 0.000 2.532	andard error V 0.333 0.313	/ariance 0.111 0.098	Lower limit -0.653 1.919	Upper limit 0.653 3.144	0.000 8.098	1.000 0.000		<u>Std diffi</u>	in means a	nd 95% CI	-
Depression: All tests	S in Harmon, 2004 Kadoi, 2011b	means 0.000 2.532 0.060	andard error V 0.333 0.313 0.172	Variance 0.111 0.098 0.029	Lower limit -0.653 1.919 -0.277	Upper limit 0.653 3.144 0.396	0.000 8.098 0.348	1.000 0.000 0.728	-4.00	<u>Std diff i</u>	in means a	nd 95% Cl	-
-	S in Harmon, 2004 Kadoi, 2011b	means 0.000 2.532 0.060	andard error V 0.333 0.313 0.172	Variance 0.111 0.098 0.029	Lower limit -0.653 1.919 -0.277	Upper limit 0.653 3.144 0.396	0.000 8.098 0.348	1.000 0.000 0.728			+		-
-	S in Harmon, 2004 Kadoi, 2011b	means 0.000 2.532 0.060 0.856	andard error V 0.333 0.313 0.172 0.781	/ariance 0.111 0.098 0.029 0.610 Statistics	Lower limit -0.653 1.919 -0.277 -0.675	Upper limit 0.653 3.144 0.396 2.386 study	0.000 8.098 0.348 1.096	1.000 0.000 0.728		-2.00	+	2.00	- 4.0
-	S in Harmon, 2004 Kadoi, 2011b Silbert, 2006	means 0.000 2.532 0.060	andard error V 0.333 0.313 0.172 0.781	/ariance 0.111 0.098 0.029 0.610 Statistics	Lower limit -0.653 1.919 -0.277 -0.675	Upper limit 0.653 3.144 0.396 2.386 study r Uppe	0.000 8.098 0.348 1.096	1.000 0.000 0.728		-2.00	0.00	2.00	-
-	S in Harmon, 2004 Kadoi, 2011b Silbert, 2006 <u>Study name</u>	means 0.000 2.532 0.060 0.856 Difference in means	andard error V 0.333 0.313 0.172 0.781 Standard error	/ariance 0.111 0.098 0.029 0.610 <u>Statistics</u> d Variance	Lower limit -0.653 1.919 -0.277 -0.675 sfor each Lower e limit	Upper limit 0.653 3.144 0.396 2.386 study r Uppe limit	0.000 8.098 0.348 1.096	1.000 0.000 0.728 0.273		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998	means 0.000 2.532 0.060 0.856 Difference in means -5.34	andard error V 0.333 0.313 0.172 0.781 Standarn error 0 3.33	/ariance 0.111 0.098 0.029 0.610 <u>Statistics</u> d Variance 54 1125	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675	Upper limit 0.653 3.144 0.396 2.386 study Uppe limit 4 1.23	0.000 8.098 0.348 1.096 r t <b>Z-Valu</b> 4 -1.59	1.000 0.000 0.728 0.273 e p-Value 12 0.111		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011	means 0 0.000 2.532 0.060 0.856 Difference in means -5.34 0.65	andard error V 0.333 0.313 0.172 0.781 Standar error 0 3.38 0 1.11	Variance 0.111 0.098 0.029 0.610 Statistics d Variance 54 1125 14 124	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.653 -0.277 -0.675 -0.277 -0.675 -0.277 -0.675 -0.277 -0.675 -0.277 -0.675 -0.277 -0.675 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.277 -0.575 -0.57	Upper limit 0.653 3.144 0.396 2.386 study r Uppe limit 4 1.23	0.000 8.098 0.348 1.096 t <b>Z-Value</b> 34 -1.59 34 0.58	1.000 0.000 0.728 0.273 <b>e p-Value</b> 12 0.111 3 0.560		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006	means 0 0.000 2.532 0.060 0.856 Difference in means -5.34 0.65 -1.00	andard error V 0.333 0.313 0.172 0.781 Standam error 0 3.38 0 1.1* 0 0.66	Variance 0.111 0.098 0.029 0.610 Statistics d Variance 54 1125 14 124 51 0.43	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.632 -0.277 -0.633 -0.277 -0.653 -0.277 -0.75 -0.	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Uppe limit 4 1.23 14 2.83 15 0.25	0.000 8.098 0.348 1.096 r t <b>Z-Value</b> 34 -1.59 34 0.58 35 -1.51	1.000 0.000 0.728 0.273 <b>e p-Value</b> 2 0.111 3 0.560 3 0.130		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	means 0 0.000 2.532 0.060 0.856 0.856 0.856 0.856 0.856 0.856 0.400 0.400	andard error v 0.333 0.313 0.172 0.781 standar error 0 3.38 0 1.11 0 0.66 0 0.25	Variance 0.111 0.098 0.029 0.610 <u>Statistics</u> 4 Variance 54 1125 54 11	Lower limit -0.653 1.919 -0.277 -0.675 for each Lower e limit 51 -11.91 1 -1.53 7 -229 5 -0.17	Upper limit 0.653 3.144 0.396 2.386 2.386 study Upper limit 4 1.23 4 2.83 5 0.24 2 0.97	0.000 8.098 0.348 1.096 <b>Z-Value</b> 4 -1.59 34 0.58 35 -1.51 72 1.37	1.000 0.000 0.728 0.273 <b>e p-Value</b> 2 0.111 3 0.550 3 0.130 1 0.170		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006	means 0 0.000 2.532 0.060 0.856 Difference in means -5.34 0.65 -1.00	Standard         V           0.333         0.313           0.313         0.172           0.781         0.781           Standarderror         0.338           0         3.38           0         1.17           0         0.68           0         0.28           0         0.23           0         0.338	Variance 0.111 0.098 0.029 0.610 <u>Statistics</u> 4 Variance 54 11.25 14 1.24 14 1.24 14 1.24 10.43 12 0.68 10 12 12 12 14 1.24 1.24 1.24 1.24 1.24 1.	Lower limit -0.653 1.919 -0.277 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.775 -0.77	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Upper limit 4 1.23 14 2.83 15 0.29 19 1.23	0.000 8.098 0.348 1.096 t Z-Value 4 -1.59 34 0.58 35 -1.51 72 1.37 39 1.32	1.000 0.000 0.728 0.273 <b>e p-Value</b> 12 0.111 3 0.560 3 0.130 1 0.170 5 0.185		-2.00	0.00	2.00	-
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	means 0 0.000 2.532 0.060 0.856 Difference in means -5.34 0.65 -1.00 0.40 0.40	Standard         V           0.333         0.313           0.313         0.172           0.781         0.781           Standarderror         0.338           0         3.38           0         1.17           0         0.68           0         0.28           0         0.23           0         0.338	Variance 0.111 0.098 0.029 0.610 <u>Statistics</u> 4 Variance 54 11.25 14 1.24 14 1.24 14 1.24 10.43 12 0.68 10 12 12 12 14 1.24 1.24 1.24 1.24 1.24 1.	Lower limit -0.653 1.919 -0.277 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.775 -0.77	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Upper limit 4 1.23 14 2.83 15 0.29 19 1.23	0.000 8.098 0.348 1.096 t Z-Value 4 -1.59 34 0.58 35 -1.51 72 1.37 39 1.32	1.000 0.000 0.728 0.273 <b>e p-Value</b> 12 0.111 3 0.560 3 0.130 1 0.170 5 0.185	-4.00	-2.00	e in means	2.00	
-	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	means 0 0.000 2.532 0.060 0.856 Difference in means -5.34 0.65 -1.00 0.40 0.40	Standard         V           0.333         0.313           0.313         0.172           0.781         0.781           Standarderror         0.338           0         3.38           0         1.17           0         0.68           0         0.28           0         0.23           0         0.338	Variance 0.111 0.098 0.029 0.610 <u>Statistics</u> 4 Variance 54 11.25 14 1.24 14 1.24 14 1.24 10.43 12 0.68 10 12 12 12 14 1.24 1.24 1.24 1.24 1.24 1.	Lower limit -0.653 1.919 -0.277 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.675 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.777 -0.775 -0.77	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Upper limit 4 1.23 14 2.83 15 0.29 19 1.23	0.000 8.098 0.348 1.096 t Z-Value 4 -1.59 34 0.58 35 -1.51 72 1.37 39 1.32	1.000 0.000 0.728 0.273 <b>e p-Value</b> 12 0.111 3 0.560 3 0.130 1 0.170 5 0.185		-2.00	0.00	2.00	-   4.00
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	means 0 0.000 2.532 0.060 0.856 0.856 0.856 0.655 -1.00 0.40 0.400 0.50	Standard         V           0.333         0.313           0.313         0.172           0.781         0.172           0.781         0.172           0.333         0.172           0.172         0.333           0.172         0.333           0.172         0.333           0.172         0.333           0.172         0.333           0.172         0.333           0.172         0.333           0.172         0.333	Variance 0.111 0.098 0.029 0.610 <u>Statistics</u> 4 Variance 54 11.25 14 1.24 14 1.24 14 1.24 15 0.43 20.068 7 0.14	Lower limit -0.653 1.919 -0.277 -0.675 for each Lower e limit i1 -11.91 i1 -153 i5 -0.17 i2 -0.23 i7 -0.56	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Uppe limit 4.12: 4.2.8: 5.0.22 2.9: 5.0.22 2.9: 9.12: 7.0.8:	0.000 8.098 0.348 1.096 t Z-Value 4 -1.59 34 0.58 35 -1.51 72 1.37 39 1.32	1.000 0.000 0.728 0.273 <b>e p-Value</b> 12 0.111 3 0.560 3 0.130 1 0.170 5 0.185	-4.00	-2.00	e in means	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Mathew, 2007 Swaminathan, 2002	means 0 0.000 2.532 0.060 0.856 0.856 0.856 -0.00 0.40 0.50 0.13	andard error v 0.333 0.313 0.172 0.781 0.781 0.066 0.025 0.035 0.035 0.035	Variance 0.111 0.098 0.029 0.610 Statistics 4 Variance 4 Variance 4 1.25	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.23 -0.7 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.25 -0.27 -0.675 -0.77 -0.565 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 1.02 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 2	0.000 8.098 0.348 1.096 <b>r</b> <b>z-Valu</b> 34 -1.59 34 0.58 35 -1.51 72 1.37 39 1.32 77 0.36	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.185 5 0.715	-4.00	-2.00	e in means	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Study name.	means         0.000           2.532         0.060           0.856         0.856           Difference         in means           -5.34         0.65           -1.00         0.40           0.50         0.13	andard error v 0.333 0.313 0.172 0.781 v Standarn error 0 3.38 0 1.17 0 0.66 0 0.25 0 0.35 0 0.35 v standard error v v	Ariance 0.111 0.098 0.029 0.610 Statistics 4 Variance 4 1.25 1.25 1	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.77 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.23 -0.277 -0.675 -0.77 -0.565 -0.77 -0.565 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -0.77 -0.566 -	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 1.02 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097 1.02 2.097	0.000 8.098 0.348 1.096 <b>Z-Value</b> 94 -1.59 94 0.58 6 -1.51 72 1.37 39 1.32 77 0.36	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 5 0.175 5 0.715	-4.00	-2.00	e in means	2.00	
Depression: All tests Education (years) .VEF %	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002	means 0 0.000 2.532 0.060 0.856 0.856 0.856 -1.00 0.40 0.50 0.13	andard error V 0.333 0.313 0.172 0.781 Standard error 0 0.333 0.111 0.660 0.022 0.033 0.035 0.035	Ariance 0.111 0.098 0.029 0.610 Statistics 4 Variance 4 1.25 1.25 1	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.77 -0.675 -0.566 -0.77 -0.566 -0.	Upper limit 0.653 3.144 0.396 2.386 2.386 r Upper limit 4 1.22 4 2.82 4 2.82 4 2.82 4 2.82 4 2.82 4 2.82 4 2.82 1 1.114	0.000 8.098 0.348 1.096 <b>r</b> <b>z-Value</b> 4 -1.59 4 0.58 5 -1.51 7 0.36 -1.21 7 0.36	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 3 0.130 5 0.185 5 0.715 Value 0.208	-4.00	-2.00	e in means	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002	means 0 0.000 2.532 0.060 0.856 0.856 0.856 0.856 -1.00 0.40 0.50 0.13	Andard error 0.333 0.313 0.172 0.781 0.781 0.781 0.781 0.781 0.332 0.112 0.660 0.033 0.033 0.033 0.033 0.033	Statistics           0.111           0.098           0.029           0.610           Statistics           d           Variance           54           11.25           4           124           20.08           7           0.14           36           0.12           atistics for et 5.910	Lower limit -0.653 1.919 -0.277 -0.675 for each Lower e limit 1 -11.91 1 -153 5 -0.17 2 -0.229 5 -0.17 2 -0.26 -0.277 -0.675 e limit 1 -1.53 -7 -0.56 -0.277 -0.675 -0.77 -0.56 -0.77 -0.75 -0.7	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 1.027 2.037 7.082 7.082 7.082 7.082 7.082 7.082	0.000 8.098 0.348 1.096 r t <b>Z-Value</b> 4 -1.59 4 0.58 5 -1.51 72 1.37 19 1.32 7 0.36 -Value p-1 -1.259 0.411	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.135 5 0.135 5 0.715	-4.00	-2.00	0.00	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002	means         0.000           2.532         0.060           0.856         0.856           Difference         1.000           0.53         0.40           0.55         0.13           0.66         0.40           0.55         0.13           0.67         0.13           0.55         1.000           0.500         1.000	Standard         N           0.333         0.313           0.313         0.172           0.781         0.781           Standard         0.338           0         1.19           0         0.333           0         1.11           0         0.66           0         0.338           0         0.338           0         0.338           1.519         2.431           1.519         2.431	Ariance 0.111 0.098 0.029 0.610 Statistics Ariance 4 1125 4 125 4 125 4 125 4 125 4 126 5 0.08 7 0.14 56 0.12 Ariance 2.54 5.510 2.304	Lower limit -0.653 1.919 -0.277 -0.675 stor each Lower e limit i1 -11.91 i1 -153 i5 -0.17 i2 -0.23 i7 -0.56 each stud ower U limit I -5.114 -3.765 -2.075	Upper limit 0.653 3.144 0.396 2.386 2.386 study r Upper limit 4 1.2: 4 2.8: 5 0.2! 7 0.8: 7 0	0.000 8.098 0.348 1.096 * * Z-Value 94 -1.59 94 0.58 95 -1.51 72 1.37 199 1.32 77 0.388 * * Value p-1 -1.259 0.411 0.593	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.185 5 0.715 Value 0.208 0.881 0.553	-4.00	-2.00	0.00	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002	means 0 0.000 2.532 0.060 0.856 0.856 0.856 0.856 -1.00 0.40 0.50 0.13	Andard error 0.333 0.313 0.172 0.781 0.781 0.781 0.781 0.781 0.332 0.112 0.660 0.033 0.033 0.033 0.033 0.033	Variance           0.111           0.098           0.029           0.610           statistics           d           Variance           id           Variance           id           variance           id           variance           id           variance           id           variance           id           distics for 4           issics for 4           5:91           2:324           6:802	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.17 -2.29 5 -0.17 -2.29 5 -0.17 -2.29 5 -0.17 -2.29 5 -0.17 -0.56 -0.17 -2.29 -0.56 -0.17 -2.29 -0.56 -0.17 -2.29 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.55 -0.17 -0.56 -0.17 -0.56 -0.17 -0.55 -0.17 -0.56 -0.17 -0.57 -0.17 -0.56 -0.17 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.17 -0.56 -0.17 -0.17 -0.56 -0.17 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.17 -0.56 -0.57 -0	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 1.027 2.037 7.082 7.082 7.082 7.082 7.082 7.082	0.000 8.098 0.348 1.096 r t <b>Z-Value</b> 4 -1.59 4 0.58 5 -1.51 72 1.37 19 1.32 7 0.36 -Value p-1 -1.259 0.411	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.135 5 0.135 5 0.715	-4.00	-2.00	0.00	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002	means         0.000           2.532         0.060           0.856         0.856           Difference in means         -5.34           -0.505         -1.00           0.40         0.50           0.133         -1.00           wifference sin means         -2.000           1.000         0.500           2.000         1.000           0.500         2.000	andard error 0.333 0.313 0.172 0.781 0.781 0.781 0.781 0.066 0.025 0.033 0.066 0.033 0.033 0.033 0.035 0.033 0.035	Ariance 0.111 0.098 0.029 0.610 Statistics Variance Variance 4 1.125 4 1.25 1.12 5 5 1.12 5 1.12 5 1.12 5 1.	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.77 -0.237 -0.237 -0.56 -0.77 -0.56 -0.237 -0.56 -0.237 -0.56 -0.237 -0.56 -0.237 -0.56 -0.277 -0.56 -0.174 -0.575 -0.174 -0.56 -0.174 -0.56 -0.174 -0.575 -0.174 -0.575 -0.174 -0.575 -0.174 -0.575 -0.174 -0.575 -0.175 -0.175 -0.175 -0.175 -0.175 -0.175 -0.175 -0.175 -0.112 -1.025 -0.125 -0.125 -0.175 -0.112 -0.255 -0.175 -0.112 -0.255 -0.175 -0.112 -0.255 -0.175 -0.112 -0.255 -0.175 -0.112 -0.255 -0.112 -0.255 -0.112 -0.255 -0.112 -0.255 -0.112 -0.255 -0.112 -0.255 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125 -0.112 -0.125	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 1.114 4.2.8 5.024 2.0.97 1.22 2.0.97 1.22 7.0.82 1.114 5.785 3.875 7.112	0.000 8.098 0.348 1.096 7 2 Z-Value 94 -1.59 94 0.58 16 -1.51 72 1.37 19 1.32 77 0.36 -Value p-1 -1.259 0.411 0.553 0.767	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.185 5 0.715 Value 0.206 0.681 0.443	-4.00	-2.00	0.00	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Silbert, 2006 Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Swaminathan, 2002 Swaminathan, 2002	means 0 0.000 2.532 0.060 0.856 0.856 0.856 0.655 -1.00 0.40 0.50 0.40 0.50 0.13 0.13 0.13 0.13	andard error 0.333 0.313 0.172 0.781 0.781 0.781 0.330 0.117 0.066 0.025 0.035 0.035	Ariance 0.111 0.098 0.029 0.610 Statistics Variance Variance 4 1.125 4 1.25 1.12 5 5 1.12 5 1.12 5 1.12 5 1.	Lower limit -0.653 1.919 -0.277 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.675 -0.77 -0.675 -0.566 -0.277 -0.566 -0.275 -0.275 -0.275 -0.275 -0.217 -0.256 -0.217 -0.217 -0.256 -0.217 -0.256 -0.217 -0.256 -0.217 -0.257 -0.217 -0.256 -0.217 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0.257 -0.217 -0	Upper limit 0.653 3.144 0.396 2.386 2.386 2.386 2.386 2.386 1.114 5.05 2.0.97 1.23 7.0.82 2.0.97 1.23 7.7 0.82 2.0.97 1.23 7.7 0.82 2.3855 2.3855 2.385 2.385 2.385 2.385 2.38	0.000 8.098 0.348 1.096 <b>Z-Value</b> 94 -1.59 94 0.58 6 -1.51 72 1.37 79 1.32 77 0.36 <b>-Value p-1</b> -1.259 0.411 0.59 0.411 0.59	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.185 5 0.715 Value 0.208 0.881 0.553 0.443 0.311	-4.00	-2.00	0.00	2.00	
Education (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Study name Kadoi, 2005 Kadoi, 2007 Kadoi, 2005 Kadoi, 2007 Kadoi, 2007 Kadoi, 2007 Braekken, 1998	means 0 0.000 2.532 0.060 0.856 0.856 0.856 -1.00 0.40 0.50 0.13 *#ference 5 in means - 0.40 0.50 0.13	andard error 0.333 0.313 0.172 0.781 <b>Standar</b> error 0.333 0.172 0.781 <b>Standar</b> error 0.333 0.112 0.066 0.025 0.035 0.035 0.035 1.518 2.451 1.518 2.455 1.3513	Ariance 0.111 0.098 0.029 0.610 Statistics 4 Variance 4 1.25 1.25	Lower limit -0.653 1.919 -0.277 -0.675 for each Lower e limit 1 -11.91 1 -153 7 -229 5 -0.17 2 -0.23 7 -0.56 each stud cover U limit -5.114 -3.765 -2.075 -3.112 -1.028 -1.038 -1.	Upper limit 0.653 3.144 0.396 2.386 2.386 r Upper limit 4 1.2: 4 2.8: 4 2.8: 1.114 5.75 3.875 3.975 3.975 3.975 3.975 3.975 3.975 3.975 3.975 3.9	0.000 8.098 0.348 1.096 <b>z-Value</b> 4 -1.59 4 0.58 5 -1.51 7 1.32 7 0.36 <b>-Value</b> p-1 -1.259 0.411 0.59 0.767 1.0767 1.0767 1.0767	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 3 0.130 5 0.185 5 0.715 Value 0.208 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.881 0.811 0.881 0.8310 0.8310 0.83100000000000000000000000000000000000	-4.00	-2.00	e in means	2.00	
ducation (years)	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Study name Kadoi, 2005 Kadoi, 2007 Kadoi, 2005 Kadoi, 2007 Kadoi, 2007 Kadoi, 2007 Braekken, 1998	means         0.000           2.532         0.060           0.856         0.856           Difference         1.000           0.40         0.50           0.13         0.40           0.50         0.13	Andard error 0.333 0.313 0.172 0.781 Standar error 0.332 0.112 0.781 0.066 0.033 0.033 0.025 0.033 0.033 0.033 0.172 0.781 0.066 0.033 0.033 0.172 0.781 0.555 1.559 2.431 1.518 2.609 2.431 1.518 2.609 1.518 2.639 1.444	Ariance 0.111 0.098 0.029 0.610 Statistics 4 Variance 4 1.25 1.25	Lower limit -0.653 1.919 -0.277 -0.675 for each Lower e limit 1 -11.91 1 -153 7 -229 5 -0.17 2 -0.23 7 -0.56 each stud cover U limit -5.114 -3.765 -2.075 -3.112 -1.028 -1.038 -1.	Upper limit 0.653 3.144 0.396 2.386 2.386 1.014 4.122 2.091 9.122 2.091 9.122 2.091 9.122 2.091 9.122 2.091 9.122 2.091 9.122 2.091 9.122 2.091 9.122 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.082 2.095 7.005 7.095 7.005	0.000 8.098 0.348 1.096 <b>r</b> <b>z-Value</b> 4 -1.59 4 0.58 5 -1.51 72 1.37 9 1.32 7 0.36 <b>-Value p-1</b> -1.259 0.411 0.553 0.765 1.014 0.521 0.593	1.000 0.000 0.728 0.273 2 0.111 3 0.560 3 0.130 1 0.170 5 0.185 5 0.715 Value 0.206 0.681 0.653 0.443 0.336	-4.00	-2.00	e in means	2.00	

Intra-Operative (Continuous)															
ACC time (mins)	Study name         Statistics for each study									Difference in means and 95% Cl					
		Difference in means	Standard	Variance	Lower limit	Upper limit	Z-Value	p-Value							
	Braekken, 1998	8.086				29.282	0.748	0.455	Ľ.	4	11	T.			
	Mathew, 2006	-4.300				5.724	-0.841	0.400	$\sum$			-	- (		
	Mathew, 2007	-1.900				2.131	-0.924	0.356		(1997) 					
	Swaminathan, 2002					5.568	0.036	0.971		-		-			
		-1.291				1.763	-0.829	0.407		-					
									-10.00	-5.00	0.00	5.00	10.00		
CPB time (mins)	Study name	me Statistics for each study								Difference	e in means :	and 95% Cl			
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value							
	Developed 4000								L2			L	J		
	Braekken, 1998 Kadoi, 2005	5.159				39.094 15.132	0.298	0.766	< C						
	Kadoi, 2003	3.000				12.181	0.640	0.522			-		- 1		
	Kadoi, 2011b	9.900					1.640	0.101			-	- 18 .	-		
	Mathew, 2006	-5.000				9.647	-0.669		k—	<b>•</b>			285		
	Mathew, 2007	-2.700					-0.907	0.364				-			
	Swaminathan, 2002						-0.437		K		0 10 <u>29</u>	Carly 1	-		
		2.149	2.343	3 5.490	-2.444	6.741	0.917	0.359	-10.00	-5.00	0.00	5.00	10.00		
Number of grafts	Study name			Statistics	or each s	tudy			Difference in means and 95% CI						
		Difference	Standard		Lower	Upper									
		in means	error	Variance	limit	limit	Z-Value	p-Value							
	Dieleman, 2009	0.020	0.244	0.059	-0.458	0.497	0.081	0.935	- 1	-	-+-	_			
	Mathew, 2006	-0.200	0.164	0.027	-0.521	0.121	-1222	0.222							
	Mathew, 2007	0.000	0.083	0.007	-0.163	0.163	0.000	1.000							
	Swaminathan, 2002						-0.913								
		-0.055	0.056	0.004	-0.171	0.062	-0.920	0.358	 -1.00	-0.50	0.00	0.50	1.00		
Fotal Microemboli	Study name			Statistics	oreache	tudy				Std diff	in means a	and 0.5% Cl			
	study name	Std diff	Standard	Statistics	Lower	Upper				Stutim	in means a	nu 95% C			
		inmeans	error	Variance	limit	limit	Z-Value	p-Value							
	Braekken, 1998	-0.770	0.778	0.605	-2.294	0.753	-0.991	0.322	- K-			- 1			
	Liu, 2009	-0.076	0.244	0.059	-0.553	0.402	-0.310	0.756			_8				
	Rodriguez, 2010	-0.310	0.226	0.051	-0.752	0.133	-1.372	0.170		-					
	Royse, 2000	-1.491	0.535	0.287	-2.541	-0.442	-2.786	0.005	< -	-	-				
		-0.459	0.258	0.067	-0.965	0.048	-1.775	0.076							
									-2.00	-1.00	0.00	1.00	2.0		
Post-Operative (Continuous)															
LOS in ICU (days)	Study name		S	tatistics for	each stu	dy				Difference	e in means	and 95% Cl			
200 m 100 (awj0)		ifference S in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value							
	Baba, 2007	0.880	0.276	0.076	0.338	1.422	3.185	0.001	1	I.	É é		a 1		
	Dieleman, 2009	-0.470	0.371	0.137	-1.197	0.257	-1.268	0.205							
		0.228	0.675	0.455	-1.095	1.550	0.337	0.736					<u></u>		
										1000					

Figure S6. Funnel pl	ots for statistically significant analyses in regard to mid-term	Egger's Test	Trim and Fill				
-	et-CABG, and results of publication bias/small-study effect nore than 10 studies were available.	p value Intercept (1-tailed)	No. imputed OR/MD† 95%CI studies /SMD‡				
Preoperative (Categorica	al)						
Depression	Only 2 studies, could not produce funnel plot						
Preoperative (Continuou	is)						
Cognition: All tests	Funnel Plot of Standard Error by Std diff in means						

## Figure S7. Forest plots for long-term cognitive decline post-CABG analyses.

Forest Plot
Study name Statistics for each study Odds ratio and 95% Cl
Odds Lower Upper ratio limit limit Z-Value p-Value
Silbert, 2008 0.824 0.385 1.763 -0.499 0.618
Trubnikova, 2014 1.339 0.563 3.189 0.660 0.509
1.018 0.574 1.803 0.060 0.952
0.1 0.2 0.5 1 2 5 10
Study name         Statistics for each study         Odds ratio and 95% CI
Odds Lower Upper
ratio limit limit Z-Value p-Value
Dieleman, 2009 1.064 0.346 3.277 0.109 0.913
Lachmann, 2018 1.623 0.788 3.345 1.313 0.189
1.435 0.781 2.636 1.164 0.245
0.1 0.2 0.5 1 2 5 10
Study name         Statistics for each study         Odds ratio and 95% CI
Odds Lower Upper ratio limit limit Z-Value p-Value
Dieleman, 2009 0.819 0.365 1.837 -0.485 0.628
1.170 0.279 4.906 0.215 0.830
0.1 0.2 0.5 1 2 5 10
Study name         Statistics for each study         Odds ratio and 95% CI
Odds Lower Upper ratio limit limit Z-Value p-Value
Dieleman, 2009 1.612 0.758 3.427 1.241 0.215
Lachmann, 2018 1.163 0.685 1.975 0.560 0.576
1.296 0.840 1.998 1.171 0.241
0.1 0.2 0.5 1 2 5 10
Study name         Statistics for each study         Difference in means and 95% CI
Difference Standard Lower Upper
in means error Variance limit limit Z-Value p-Value Dieleman, 2009 3.300 1.730 2.992 -0.090 6.690 1.908 0.056
Kok 2017 -1.500 3.073 9.444 -7.523 4.523 -0.488 0.625
1.572 2.304 5.308 -2.944 6.088 0.682 0.495
-8.00 -4.00 0.00 4.00 8.00

Number of grafts	Study name	Statistics for each study								Difference in means and 95% Cl					
		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value							
	Dieleman, 2009	0.047	0.192	0.037	-0.330	0.424	0.243	0.808	1	-		-	1		
	Kok, 2017	0.008	0.249	0.062	-0.480	0.496	0.034	0.973		<u>~</u>	-	5			
		0.032	0.152	0.023	-0.266	0.331	0.213	0.832				-	243		
									-1.00	-0.50	0.00	0.50	1.00		