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SYSTEMATIC REVIEW AND META-ANALYSIS

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

Danielle Greaves , BAppSc (Hons); Peter J. Psaltis, PhD; Daniel H. J. Davis , PhD; Tyler J. Ross , BPsych (Hons); Erica S. Ghezzi , BPsych (Hons); Amit Lampit , PhD; Ashleigh E. Smith , PhD; Hannah A. D. Keage , PhD

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 presence of delirium and increased days in the intensive care unit. Presence of depression preoperatively was 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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Key Words: cognitive decline ■ coronary artery bypass grafting ■ delirium ■ meta-analysis

oronary artery bypass grafting (CABG) surgery is the main treatment for multivessel coronary disease and remains one of the most common cardiac procedures worldwide. CABG has low mortality rates, and improves coronary vascularization and cardiac function. However, CABG is associated with high rates of postoperative cognitive impairments, including delirium.⁴⁻⁶

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

Correspondence to: Danielle Greaves, BAppSc (Hons), GPO Box 2471, Adelaide, South Australia, Australia 5001. E-mail: danielle.greaves@mymail.unisa.edu.au For Sources of Funding and Disclosures, see page 12.

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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. 4

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.⁷ 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.⁸⁻¹¹ Research attempting to

prevent these post-CABG cognitive outcomes has been largely unsuccessful, including pharmacological, anesthetic intervention, and surgical techniques. 12–16 There has been some evidence of therapeutic effect for advanced surgical methods, such as hypothermia and increasing systemic perfusion intraoperatively. 17 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)^{15,16} and the effect of pharmacological and anesthetic interventions on postoperative delirium. 18,19 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.²⁰ 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.⁴ 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,^{21,22} 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.^{23,24} 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 I^2 statistic was used to

express the proportion of between-study heterogeneity out of total variance and was classified as low ($I^2=25\%-50\%$), moderate ($I^2=50\%-75\%$), or high ($I^2\ge75\%$), using classification criteria suggested by Higgins et al. ²⁵ Total between-study variance was quantified using τ^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 ≥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 ≥ 0.20 , ≥ 0.50 , and ≥ 0.80 are considered as small, moderate, and large, respectively.²⁶ For cognitive decline post-CABG, analyses 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 (eg. 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.²⁷ When at least 10 studies were available for analyses, small study effect was formally assessed using the Egger test of the intercept.²⁸ When there was evidence for small study effect (1-tailed P<0.1), we used the Duvall and Tweedie²⁹ 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 quidelines, 30 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 (eg. 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 interquartile 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).

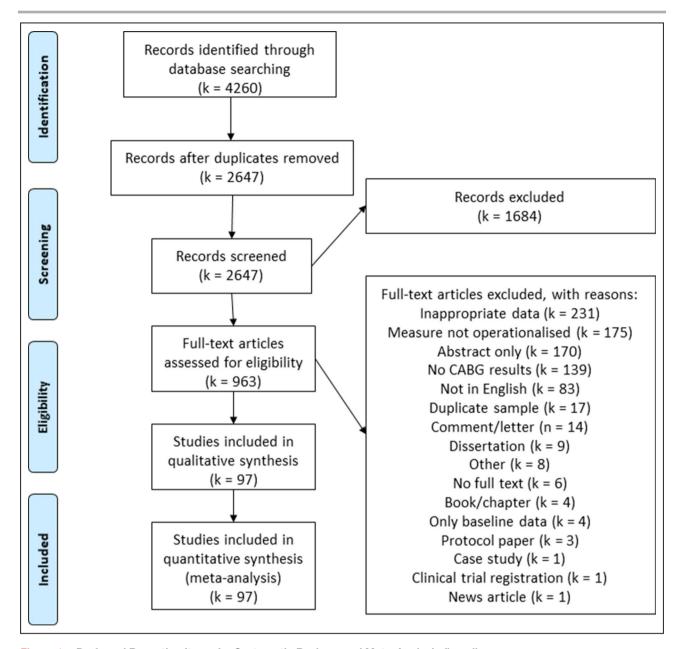


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram. CABG indicates coronary artery bypass grafting.

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^2 range, 0–98.40; τ^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/m², 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/m², dyslipidemia/hyperlipidemia,

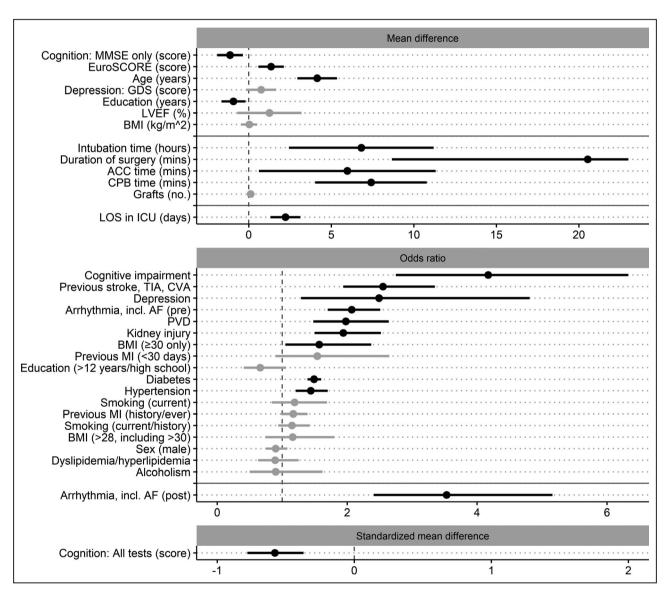


Figure 2. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting delirium. Factors grouped according to the primary pooled estimate of the analysis (mean difference [MD], odds ratio, or standardized MD [SMD]), where solid gray horizontal lines indicate 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 Cls 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 Cls 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, $R^2 = 0.50$) 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^2 range, 0-92.85; τ^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: β =-0.88, Z=-2.24, P=0.025, R^2 =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 (12 range, 0–68.84; 22 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.

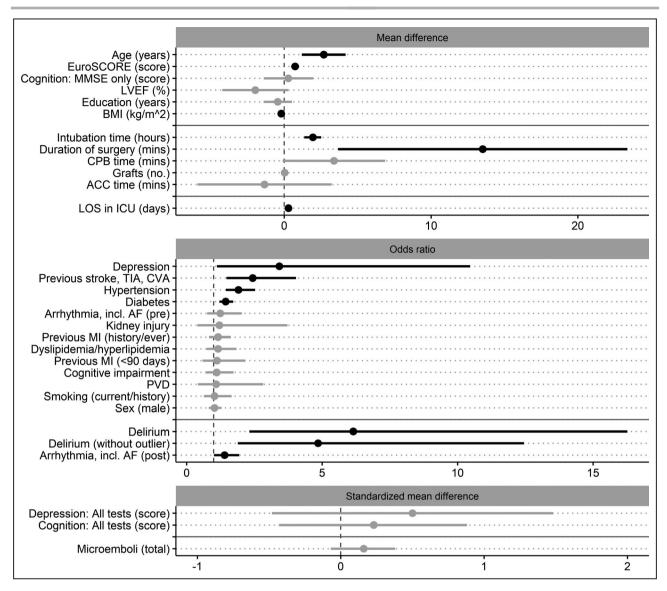


Figure 3. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting acute cognitive decline.

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,

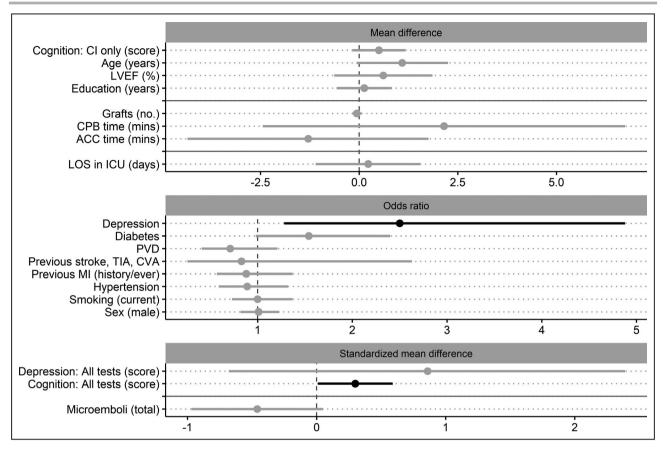


Figure 4. Forest plots of pooled estimates for risk or protective factors of post–coronary artery bypass grafting midterm cognitive decline.

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. ^{31,32} 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. Most published delirium prediction tools are based on individual clinical studies with low statistical power, decreasing their generalizability. 33-36 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.⁹ Recent editorials^{37,38} have highlighted

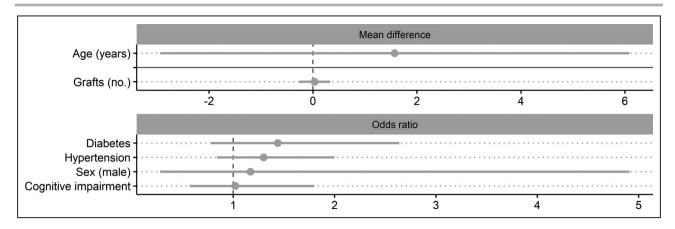


Figure 5. Forest plots of pooled estimates for risk or protective factors of post-coronary artery bypass grafting long-term cognitive decline.

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.42

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 (I^2 , 93.32–96.08; τ^2 , 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.⁴⁴ 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 decline³⁷ and greatly increases the risk of incident dementia.⁴⁸ 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

decline is seen in nearly 40% of patients 1 to 5 years post-CABG.⁴ The presence of cognitive decline is associated with decreased quality of life, functional capacity, and increased rates of depression.⁷ In addition, longer-term cognitive decline can lead to a loss of support networks, such as friends and neighbors, and can strain familial relationships.⁴⁹ 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 (eg. AF, dialysis, reintubation, and stroke).50 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. 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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Affiliations

From the Cognitive Ageing and Impairment Neurosciences Laboratory, Justice and Society Academic Unit, University of South Australia, Adelaide,

Australia (D.G., T.J.R., E.S.G., A.E.S., H.A.K.); Vascular Research Centre, Lifelong Health Theme, South Australian Health and Medical Research Institute, Adelaide, Australia (P.J.P.); Adelaide Medical School, University of Adelaide, Adelaide, Australia (P.J.P.); Department of Cardiology, Royal Adelaide Hospital, Central Adelaide Local Health Network, Adelaide, Australia (P.J.P.); Medical Reasearch Council Unit for Lifelong Health and Ageing Unit at UCL, London, United Kingdom (D.H.D.); Academic Unit for Psychiatry of Old Age, Department of Psychiatry, University of Melbourne, Melbourne, Australia (A.L.); Department of Neurology, Charité—Universitätsmedizin Berlin, Berlin, Germany (A.L.); and Alliance for Research in Exercise, Nutrition and Activity, Allied Health and Human Performance Academic Unit, University of South Australia, Adelaide, Australia (A.E.S.).

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Disclosures

None.

Supplementary Material

Data S1 Tables S1-S9 Figures S1-S7 References 51-146

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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 ^{21, 22}.

2 points: Sufficiently fulfilled

1 point: Partially fulfilled or unclear0 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:			
1000.			

*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).

Overall Appraisal Grade: /12

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

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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
Variable	k (n)	OR/MD†/ SMD‡	95%CI	p value	\mathbf{I}^2	Tau²	effect size 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 ≥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

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	k (n)	OR/MD†/	95%CI	p value	\mathbf{I}^2	Tau ²	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
	1						

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‡	-0.07—0.38	.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

		Pooled 1	Estimate		Heterog	geneity	Effect size
Variable	k (n)	OR/MD†/	95%CI	p value	\mathbf{I}^2	Tau ²	SMD
		SMD‡					
Pre-Operative (Categorical)							
Depression	2 (471)	2.50	1.28—4.88	.007	0	0	0.51
Diabetes	10 (2046)	1.54	0.98—2.40	.059	61.33	0.28	0.24
Sex (male)	12 (2599)	1.01	0.82—1.23	.965	0	0	0.00
Hypertension	12 (2350)	0.89	0.59—1.32	.558	69.32	0.31	0.07
Previous MI history/ever	3 (975)	0.88	0.57—1.37	.580	41.32	0.06	0.07
Previous stroke, TIA, CVA	2 (761)	0.83	0.26—2.63	.748	0	0	0.11
p PVD	2 (761)	0.71	0.41—1.21	.209	0	0	0.19
Smoking (current)	5 (1006)	1.00	0.73—1.37	.983	0	0	0.00
Pre-Operative (Continuous)							
Age (years)	12 (2093)	1.09†	-0.06—2.25	.063	29.21	1.12	0.13
Cognition: All tests	3 (855)	0.30‡	0.01—0.59	.041	68.84	0.04	0.30
Cognition: CI only	2 (795)	0.50†	-0.17—1.17	.146	89.28	0.21	0.43
Depression: All tests Education (years)	3 (429)	0.86‡	-0.68—2.39	.273	96.08	1.75	0.86
Education (years)	5 (950)	0.13†	-0.57—0.83	.715	44.26	0.24	0.05
LVEF %	7 (1266)	0.61†	-0.63—1.86	.336	0	0	0.06
Intra-Operative (Continuous)							
ACC time (mins)	4 (890)	-1.29†	-4.35—1.76	.407	0	0	0.06
CPB time (mins)	7 (1266)	2.15†	-2.44—6.74	.359	28.63	10.41	0.06
Number of grafts	4 (1124)	-0.06†	-0.17—0.06	.358	0	0	0.06

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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	\mathbf{I}^2	Tau ²	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
Intra-Operative (Continuous)							
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† and SMD‡. 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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Wu M, Liang Y, Dai Z, Wang S. Perioperative dexmedetomidine reduces delirium after cardiac surgery: A meta-analysis of randomized controlled trials. Journal	other
of Clinical Anesthesia. 2018;50:33-42	
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	protocol paper
outcomes in older men undergoing on-pump cabg. Contemporary Clinical Trials. 2012;33:730-738	
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	protocol paper
multi-vessel coronary artery bypass surgery (promiss) using multidetector computed tomography. Trials. 2008;9:44	
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	protocol paper
surgery trial. American Heart Journal. 2014;167:660-665	

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 Vear	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C(2)	C2	D.I	QA
Kei. No.	Lead Author, Year	Patients	of Males	Age	of Age	C1	C2	C3	Del	(/12)	
51	Al Tmimi, 2016	92	78	67	R: 46-86	-	-	_	X	12	
52	Baba, 2007	218	152	71.25	5.5	X	-	-	-	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.	Lood Author Voor	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA
Kei. Ivo.	Lead Author, Year	Patients	of Males	Age	of Age	CI	C2	CS	Dei	(/12)
62	deTournay-Jette, 2011	61	51	70.39	4.69	X	X	-	-	10
63	Dieleman, 2009	281	192	61.3	9	-	X	X	-	10
64	Djaiani, 2003	417	293	60.34	10	-	X	-	-	9
65	Dong, 2014	108	83	63	7.9	X	-	-	X	10
66	Eriksson, 2002	52	40	70.27	5.53	-	-	-	X	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 [†]	35	28	61.7	7.51	X	X	-	-	9
71	Harmon, 2005 [†]	36	30	64.07	N/A	X	-	-	-	12
72	Humphreys, 2016	173	148	63.47	10.1	-	-	-	X	7
73	Kadoi, 2001 [‡]	185	138	N/A	N/A	X	X	-	-	6
74	Kadoi, 2002§	60	53	62.75	8.5	_	X	-	-	9

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA
101.110.	near runor, rear	Patients	of Males	Age	of Age	O1	62		Dei	(/12)
75	Kadoi, 2003 [‡]	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) ¶	113	90	64	R: 59-71	-	-	-	X	12
81	Kazmierski, 2014 (b)¶	102	N/A	N/A	N/A	-	-	-	X	12
82	Kazmierski, 2014 (c) ¶	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.	Lood Author Voor	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA
Kei. No.	Lead Author, Year	Patients	of Males	Age	of Age	CI	C2	CS	Dei	(/12)
88	Leenders, 2018	357	304	66.20	8.84	-	-	-	X	9
89	Li, 2015	38	34	62.4	11.8	-	-	-	X	10
90	Liu, 2009	227	209	60	8	X	X	-	-	9
91	Loponen, 2008	300	237	66.17	8.89	_	-	-	X	8
92	Mardani, 2012	196	183	61.84	11.83	-	-	-	X	9
93	Mariscalco, 2012	4079	3220	67.8	9.2	_	-	_	X	12
94	Martin, 2010#	14262	10912	N/A	N/A	-	-	-	X	5
95	Martin, 2012#	8474	6391	N/A	N/A	-	-	-	X	7
96	Mathew, 2006**	121	N/A	N/A	N/A	-	X	-	-	8
97	Mathew, 2007**	677	471	61.7	10.5	-	X	-	-	9
98	Miyazaki, 2011	768	N/A	N/A	N/A	-	-	-	X	6
99	Mu, 2010	243	200	61	8.3	-	-	-	X	12
100	Mu, 2013	166	141	60	8.9	X	_		_	12

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA
Rei. No.	Lead Addior, Tear	Patients	of Males	Age	of Age	CI	C2	CS	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	X	-	-	-	10

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA
	,	Patients	of Males	Age	of Age					(/12)
114	Restrepo, 2002	13	10	65	9	X	-	-	-	10
115	Ringaitiene, 2015	99	70	67.6	7.78	-	-	-	X	10
116	Robson, 2000	124	N/A	59.44	9.25	-	X	-	-	7
117	Rodriguez, 2010	356	325	63	9	X	X	-	-	5
118	Rolfson, 1999 (a) ^{††}	75	59	N/A	N/A	-	-	-	X	12
119	Rolfson, 1999 (b) ^{††}	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 ^{‡‡}	80	62	74.9	6.2	-	-	-	X	11
124	Rudolph, 2009 ^{‡‡}	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	_	-	-	X	11

Ref. No.	Lead Author, Year	Total No. of	Total No.	Mean/Median	SD/Range/IQR	C1	C2	С3	Del	QA	
Kei. No.	Lead Addioi, Tear	Patients	of Males	Age	of Age	CI	C2	CS	Dei	(/12)	
126	Scott, 2002	103	84	64.77	1.3	X	-	-	-	12	
127	Sevuk, 2015	200	128	70.65	3.95	-	-	-	X	12	
128	Siepe, 2011	92	74	66.87	8.98	-	-	-	X	12	
129	Silbert, 2006 ^{§§}	326	252	67.9	7.6	X	X	-	-	9	
130	Silbert, 2008§§	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	X	-	-	-	9	
133	Smith, 2000	381	308	N/A	N/A	-	X	-	-	8	
134	Stump, 1996	167	138	61	10	X	-	-	-	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	С3	Del	QA
101.110.	Dead Mathor, Tear	Patients	of Males	Age	of Age	O1	62		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*	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

^{†,‡,§,¶,‡‡} Suspected overlap of samples; *,|,#,**,††,§§ 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.

Variable	Delirium Diagnosis	Pooled Estimate k (n) OR/MD*/ 95%CI			p value	Hetero I ²	ogeneity Tau ²
			SMD†				
Pre-Operative (Categorical)							
Alcoholism	No Tool		Insufficier	nt 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 ≥30 only	No Tool		Insufficier	nt Data			
	Tool	4 (419)	1.85	1.09—3.14	.023	0.00	0
Cognitive Impairment	No Tool		Insufficier	nt 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		Insufficier	nt 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

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		Delirium	Pooled Estimate			Heterogeneity		
	Variable	Diagnosis	k (n)	OR/MD*/	95%CI	p value	I^2	Tau ²
				SMD†				
		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
Downl	Pre-Operative (Continuous)							
Downloaded from http://ahaj	Age (years)	No Tool	8 (3118)	3.11*	1.50—4.72	<.001	51.30	2.31
rom ht		Tool	20 (6185)	4.52*	2.95—6.09	<.001	82.93	9.67
p://aha	BMI	No Tool		Insufficie	ent Data			
		Tool	4 (776)	0.023*	-0.6—0.65	.653	15.02	0.07
s.org by	Cognition: All tests	No Tool		Insufficie	ent Data			
on No		Tool	9 (887)	-0.58†	-0.78— -0.37	<.001	34.11	0.03
vembe	Cognition: MMSE only	No Tool		Insufficie	ent Data			
ournals.org by on November 16, 2020		Tool	7 (621)	1.14*	-1.91— -0.36	.004	77.72	0.68
20	Depression GDS	No Tool		Insufficie	ent Data			
		Tool	2 (233)	0.75*	-0.15—1.65	.101	0	0
	Education (years)	No Tool		Insufficie	ent 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
		I	I				l	

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Variable	Delirium Diagnosis	k (n)	Pooled Es OR/MD*/	stimate 95%CI	p value	Heter I ²	ogeneity Tau ²
			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
						1	

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†.

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

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

Reference No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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 >20% in ≥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 No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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 ≥ 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 No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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 No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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 No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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 ≥ 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 ≥ 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 No.	Lead Author, Year	Instruments	Definitions of Cognitive Decline and Delirium (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)

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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 3rd ed., Revised.

DSM-IV Diagnostic and Statistical Manual of Mental Disorders 4th ed.

DSM-IV-TR Diagnostic and Statistical Manual of Mental Disorders 4th 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

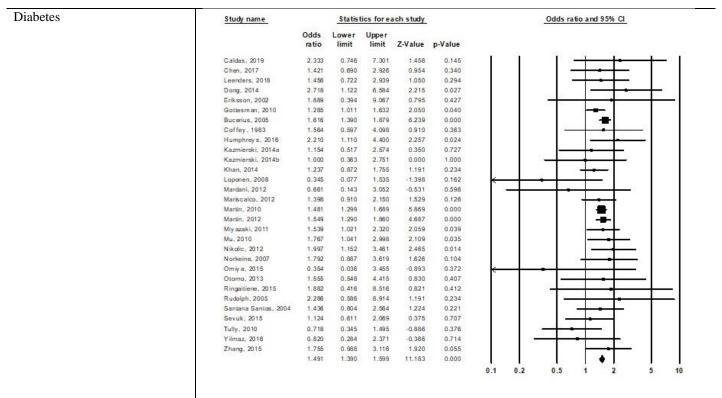
STS Accordance with Society of Thoracic Surgeons

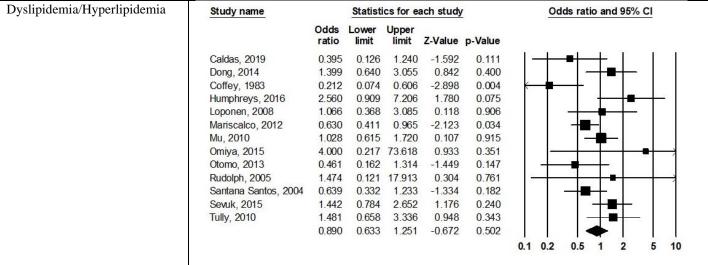
Figure S1. Forest plots for delirium post-CABG analyses.

Variable	Forest Plot											
Pre-Operative (Categorical)												
Alcoholism	Study name	9	,	Statistic	cs for e	ach stud	dy		Odds	ratio an	d 95%	CI
			Odds L ratio	ower limit		Z-Value	p-Value					
	Dong, 2014		1.057	0.362	3.084	0.101	0.919	- 1	1 -	-	—	1
	Humphreys, 2			0.390	4.206	0.407			-	— Т■		
	Loponen, 200		8.235		95.421	1.687						-
	Mu, 2010		0.557	0.265	1.171	-1.543			19 <u>-</u>			0.000
	Ringaitiene, 2				31.270			(Ξ.		,
	Rolfson, 1999		0.375	0.038	3.699			(
	110110011, 1001		0.899	0.500	1.615			Α.				
			0.000	0.000	1.010	0.007	0.721				1	- 40
								0.1	0.2 0	.5 1	2	5 10
Arrhythmia, incl. AF	Study name			Statisti	cs for ea	ach study	<u>′</u>		Odds r	atio and	95% C	1
			Odds	Lower	Upper							
			ratio	limit	limit	Z-Value	p-Value					
	Caldas, 2019		0.719	0.075	6.915	-0.286	0.775	(1 1		8	- 1
	Coffey, 1983		0.629	0.149	2.652		0.528	- I	4	-	-	
	Dong, 2014		1.310	0.519	3.303		0.568		1 1	-	_	
	Eriksson, 2002		0.258	0.013	5.012		0.371	K	 			8
	Gottesman, 2010 Kazmierski, 2014		2.363	1.647 0.597	3.392 9.343		0.000					
	Kazmierski, 2014		2.778		15.517	1.164	0.221		1 [
	Mardani, 2012	· D	4.519		19.614	2.014	0.044					
	Martin, 2010		1.883	1.522	2.330		0.000			1	-8	1
	Martin, 2012		2.070	1.575	2.720		0.000				—	
	Miyazaki, 2011		2.728	1.283	5.799	2.608	0.009			<u>=</u>	┰•	28
	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	3.454		14.872	1.664	0.096			900	- 5	
	Zhang, 2015		5.103		10.269	4.567	0.000					• 1
	_		2.068	1.700	2.514	7.277	0.000		1 1	, l	•	
								0.1	0.2 0.	5 1	2	5 10
								F	avours	A I	Favours	В
BMI >28 (including >30)	Study name		Stati	stics for	each st	udy			Odds r	atio and	95% C	
		Odds		r Uppe		lue p-Va	lue					
	0-14							r	- 1	()		. 1
	Caldas, 2019	1.31					716					
	Chen, 2017	1.39					460					
	Martin, 2010	0.70					003		1	「 <u> </u>		
	Norkeine, 2007	1.24					505		-		=	65
	Royse, 2011	2.80					022			8 0		-0
	Rudolph, 2005	1.75					420					_
	Zhang, 2015	0.69	5 0.26	66 1.8	15 -0.	743 0.	457	1.0		8 10		
	<u> </u>	1.15	8 0.74				516			2231		l I

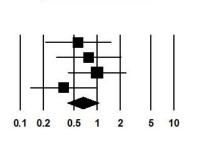
BMI ≥30 only	Study name		Statis	tics for	each st	udy	0			Odds	ratio a	nd 95%	% CI	
		Odds ratio	Lower limit			lue	p-Value							
	Caldas, 2019	1.316	0.29	9 5.78	8 0.	364	0.716	Ī	ľ	-	-	+	\rightarrow	Ĭ
	Chen, 2017	1.397	0.57	5 3.39	4 0.	738	0.460			-	000		-6	
	Norkeine, 2007	1.244	0.65	5 2.36	4 0.	667	0.505					H		
	Royse, 2011	2.800	1.16	1 6.75	2 2.	293	0.022				-			
	Rudolph, 2005	1.750	0.44	9 6.82	5 0.	806	0.420			84	10	-		
		1.573	1.04	5 2.36	8 2.	172	0.030			10	4			ļ
								0.1	0.2	0.5	1	2	5	10
Cognitive Impairment	Study name		Sta	tistics fo	or each	study	L		0	dds ra	tio an	d 95%	CI	
		Odds		er Upp it lim		alue	p-Value	į	-					
	Leenders, 2018	4.08	1 1.4	146 11.	520 2	2.656	0.008	3	Ĭ	1		_		\rightarrow
	Oldham, 2018	3.00	0 1.	123 8.0	013 2	2.192	0.028	3			-	-		-:
	Kazmierski, 2014a	7.61	9 2.5	927 19.	832	1.160	0.000)						*
	Oldham, 2015	6.11	1 1.0	056 35.	363 2	2.021	0.043	3			<u> </u>	+		-
	Rudolph, 2005	4.00	0 0.	981 16.	311	1.933	0.053	3			-	-	-	7
	Zhang, 2015	4.44		576 11.		2.997		8				32	-	7
	Rolfson, 1999b	2.31				1.462					 		_	ŧ
		4.17	0 2.	746 6.:	332 (5.700	0.000)	L	45	L	•	•	1 1
								0.1	0.2	0.5	1	2	5	10
	Study name			Statisti	cs for e	ach s	study			Odds	ratio	and 95	% CI	
			Odds ratio	Lower limit	Z-Value		per mit p-\	/alue						
	Oldham, 2018		3.984	1.158	2.19	3 13	.705	0.028	1	Î	1 1	1-		
Depression	Santana Santos, 2		1.242	0.553	0.52			0.600					-	
	Tully, 2010		3.490	1.477	2.85			0.004				_+		_
	Rolfson, 1999a		4.846	0.408		57		0.211		8	\vdash	\vdash	_	,
	5)		2.493	1.291	2.72	2 4	.811	0.006				-		
									0.1	0.2	0.5	1 2	5	10

Education>12years/high school

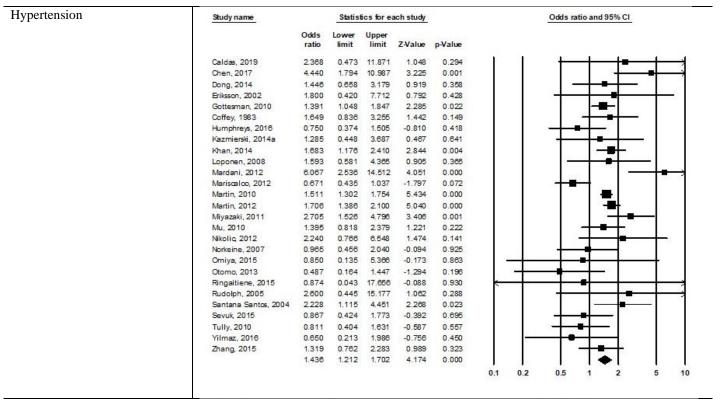


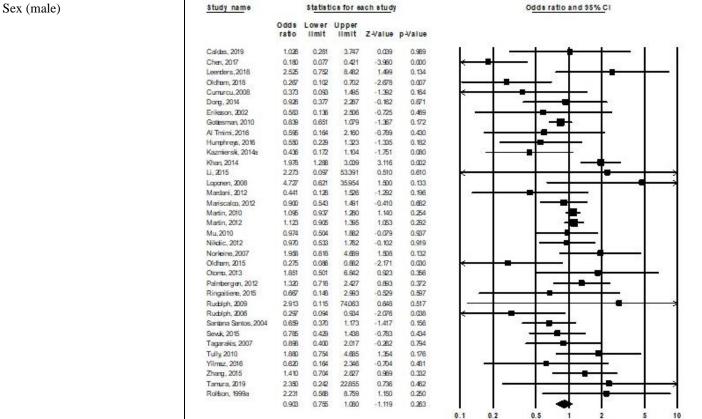


Study name		Statist	ics for ea	ach study	<u>'</u>
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Chen, 2017	0.568	0.211	1.535	-1.115	0.265
Oldham, 2018	0.779	0.291	2.086	-0.497	0.619
Rudolph, 2006	1.000	0.416	2.405	0.000	1.000
Santana Santos, 2004	0.368	0.134	1.009	-1.942	0.052
	0.658	0.407	1.064	-1.708	0.088



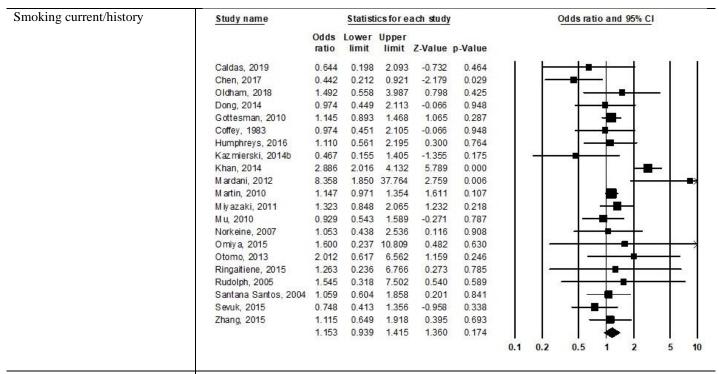
Odds ratio and 95% CI





Kidney injury	Study name		Statist	ics for e	ach study	_		Odd	ds ratio	o and 95%	% CI	
		Odds	Lower	Upper limit	Z-Value	p-Value						
	Leenders, 2018	4.744			4.104	0.000	T	1	1	1 1-	-	_
	Humphreys, 2016	1.010			0.015	0.988		-	_		_ [
	Mardani, 2012	1.973			1.525	0.127				1		
	Martin, 2010	1.918			5.019	0.000				-		
	Martin, 2012	1.607			2.755	0.006						
	Mu, 2010	1.229			0.301	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	<u> </u>	-	+	-	-	-
	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	K		-	+		628 6
	Zhang, 2015	2.492	1.030	6.032	2.025	0.043				-		
	Oh, 2017	3.060	1.120	8.360		0.029				-	-	-81
		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	/		Odd	ls rati	io and 9	5% CI	30
		odds L		Jpper								
		ratio	limit	limit	Z-Value	p-Value						
	Humphreys, 2016	0 940	0.476	1.855	-0.178	0.858	Î	Ĭ	L		ĺ	Ĩ
			0.498	6.687	0.907	0.364						_
											200	
			1.552		2.820	0.005						7
				7.547	0.672	0.502			+		-	=======================================
	Tully, 2010	1.172	0.574	2.394	0.435	0.663			200			
	9	1.543	0.898	2.653	1.570	0.116		ě.	18			
							0.1	0.2	0.5	1 2	5	10
Previous MI history/ever	-									o and 050	/ CI	
·	Study name		Statist	ics for e	ach study	_		Odd	s ratio	o and so	70 CI	
·	Study name	Odds ratio	Statist Lower limit	Upper		-A		Odo	ls ratio	o anu 30	<u>/6 CI</u>	
·		ratio	Lower limit	Upper limit	Z-Value	p-Value	1	Odd	ls ratio	_L1	<u></u> 1	1
·	Caldas, 2019	ratio 1.024	Lower limit 0.243	Upper limit 4.326	Z-Value 0.033	p-Value 0.974	1	Odd	ls ratio	and 95	<u>_</u>	1
·	Caldas, 2019 Chen, 2017	ratio 1.024 2.037	Lower limit 0.243 0.959	Upper limit 4.326 4.324	Z-Value 0.033 1.852	p-Value 0.974 0.064	1	Odd	ls ratio	o and 95	<u>-</u>	
·	Caldas, 2019 Chen, 2017 Dong, 2014	ratio 1.024 2.037 1.478	Lower limit 0.243 0.959 0.669	Upper limit 4.326 4.324 3.264	Z-Value 0.033 1.852 0.966	p-Value 0.974 0.064 0.334		Odd	ls ratio	o and 95	<u> </u>	
·	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002	1.024 2.037 1.478 1.222	Lower limit 0.243 0.959 0.669 0.336	Upper limit 4.326 4.324 3.264 4.448	Z-Value 0.033 1.852 0.966 0.304	p-Value 0.974 0.064 0.334 0.761	1	Odd	ls ratio	o and 95	 	
·	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010	ratio 1.024 2.037 1.478 1.222 1.241	Lower limit 0.243 0.959 0.669 0.336 0.978	Upper limit 4.326 4.324 3.264 4.448 1.575	Z-Value 0.033 1.852 0.966 0.304 1.773	p-Value 0.974 0.064 0.334 0.761 0.076		Odd	ls ratio		 	
·	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983	ratio 1.024 2.037 1.478 1.222 1.241 1.135	0.243 0.959 0.669 0.336 0.978 0.575	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364	p-Value 0.974 0.064 0.334 0.761 0.076 0.716	1	Odd	ls ration		 	
·	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983 Mariscalco, 2012	ratio 1.024 2.037 1.478 1.222 1.241 1.135 1.056	Lower limit 0.243 0.959 0.669 0.336 0.978 0.575 0.692	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242 1.610	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364 0.253	p-Value 0.974 0.064 0.334 0.761 0.076 0.716 0.801		Odd	ls ration		- -	
	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983 Mariscalco, 2012 Omiya, 2015	ratio 1.024 2.037 1.478 1.222 1.241 1.135 1.056 2.933	Lower limit 0.243 0.959 0.669 0.336 0.978 0.575 0.692 0.383	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242 1.610 22.463	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364 0.253 1.036	p-Value 0.974 0.064 0.334 0.761 0.076 0.716 0.801 0.300		Odd	ls ration		- -	
	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983 Mariscalco, 2012 Omiya, 2015 Ringaitiene, 2015	ratio 1.024 2.037 1.478 1.222 1.241 1.135 1.056 2.933 0.784	Lower limit 0.243 0.959 0.669 0.336 0.978 0.575 0.692 0.383 0.185	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242 1.610 22.463 3.332	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364 0.253 1.036 -0.329	p-Value 0.974 0.064 0.334 0.761 0.076 0.716 0.801 0.300 0.742		Odd	ls ratio		-	
	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983 Mariscalco, 2012 Omiya, 2015 Ringaitiene, 2015 Santana Santos, 2004	ratio 1.024 2.037 1.478 1.222 1.241 1.135 1.056 2.933 0.784 0.675	Lower limit 0.243 0.959 0.669 0.336 0.978 0.575 0.692 0.383 0.185 0.379	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242 1.610 22.463 3.332 1.203	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364 0.253 1.036 -0.329 -1.332	p-Value 0.974 0.064 0.334 0.761 0.076 0.716 0.801 0.300 0.742 0.183		Odd	Is ratio			
	Caldas, 2019 Chen, 2017 Dong, 2014 Eriksson, 2002 Gottesman, 2010 Coffey, 1983 Mariscalco, 2012 Omiya, 2015 Ringaitiene, 2015	ratio 1.024 2.037 1.478 1.222 1.241 1.135 1.056 2.933 0.784	Lower limit 0.243 0.959 0.669 0.336 0.978 0.575 0.692 0.383 0.185 0.379 0.179	Upper limit 4.326 4.324 3.264 4.448 1.575 2.242 1.610 22.463 3.332 1.203 4.129	Z-Value 0.033 1.852 0.966 0.304 1.773 0.364 0.253 1.036 -0.329	p-Value 0.974 0.064 0.334 0.761 0.076 0.716 0.801 0.300 0.742		Odd	ls ratio			

Previous stroke, TIA, CVA	Study name		Statistic	cs for ea	ch study		Odds ratio and 95% CI
		Odds L 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	
	1272	18.365		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	
	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	
	Palmbergen, 2012	7.781	2.063	29.354	3.029	0.002	
	Rolfson, 1999a	6.769	1.178	38.898	2.144	0.032	
	<u> </u>	2.546	1.936	3.350	6.680	0.000	
							0.1 0.2 0.5 1 2 5 10
PVD	Study name		Statisti	cs for ea	ch study		Odds ratio and 95% CI
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
	Caldas, 2019	0.458	0.051	4.107	-0.697	0.486	
	Leenders, 2018	1.982	0.881	4.459	1.653	0.098	
	Coffey, 1983	0.982	0.232	4.160	-0.025	0.980	
	Humphreys, 2016	1.130	0.417	3.065	0.240	0.810	
	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	2.465	1.589	0.112	
	Martin, 2012	2.159	1.765	2.642	7.478	0.000	
		10.733	3.963	29.068	4.669	0.000	
	Norkeine, 2007	2.790	1.303	5.970	2.643	0.008	
	Otomo, 2013	3.314	1.088	10.094	2.109	0.035	
	Ringaitiene, 2015	2.130	0.468	9.689	0.978	0.328	
	Sevuk, 2015	0.854	0.253	2.881	-0.254	0.799	
	TII. 2010	1.128	0.397	3.203	0.000	0.821	
	Tully, 2010	1.120			0.226	0.021	
	Tully, 2010	1.977	1.482	2.637	4.636	0.000	
	Tully, 2010						0.1 0.2 0.5 1 2 5 10
Smoking current	Study name		1.482	2.637	4.636	0.000	0.1 0.2 0.5 1 2 5 10 Odds ratio and 95% CI
moking current	2000	1.977	1.482 Statis	2.637	4.636 each stud	0.000	2000 Marie 1990 Marie
moking current	Study name	1.977 Odds ratio	1.482 Statis Lower limit	2.637	4.636 each stud	0.000 y p-Value	
moking current	Study name Caldas, 2019	Odds ratio	Statis Lower limit 3 0.069	2.637 stics for e Upper limit 9 1.697	4.636 each stud Z-Value 7 -1.312	0.000 y p-Value 0.190	
moking current	Study name Caldas, 2019 Chen, 2017	1.977 Odds ratio	Statis Lower limit 3 0.069 2 0.212	2.637 stics for e Upper limit 9 1.697 2 0.921	4.636 each stud Z-Value 7 -1.312 1 -2.179	0.000 y p-Value 0.190 0.029	2000 Marie 1990 Marie
moking current	Study name Caldas, 2019	0dds ratio 0.343 0.442	Statis Lower limit 3 0.069 2 0.212 4 0.449	2.637 stics for e Upper limit 9 1.697 2 0.921 9 2.113	4.636 Z-Value 7 -1.312 1 -2.179 3 -0.066	p-Value 0.190 0.029 0.948	2000 Marie 1990 Marie
moking current	Study name Caldas, 2019 Chen, 2017 Dong, 2014	0dds ratio 0.343 0.442 0.974	Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405	Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355	p-Value 0.190 0.029 0.948 0.175	2000 Marie 1990 Marie
moking current	Study name Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b	0.343 0.442 0.974 0.467	Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405	4.636 Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789	p-Value 0.190 0.029 0.948 0.175 0.000	2000 Marie 1990 Marie
moking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014	0dds ratio 0.343 0.442 0.97 ² 0.467 2.886	Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850	2.637 Stics for example 2 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405 6 4.132 0 37.764	Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789 4 2.759	p-Value 0.190 0.029 0.948 0.175 0.000 0.006	
moking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007	0dds ratio 0.343 0.442 0.974 0.467 2.886 8.358 1.147 1.053	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405 6 4.132 0 37.764 1 1.354 8 2.536	Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789 4 2.759 4 1.611 6 0.116	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908	
moking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600	Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809	Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789 4 2.759 4 1.611 6 0.116 9 0.482	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630	
moking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600 2.012	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237 2 0.617	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809 7 6.562	Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789 4 1.611 6 0.116 9 0.482 2 1.159	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630 0.246	2000 Marie 1990 Marie
smoking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600 2.012 1.545	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237 2 0.617 5 0.318	2.637 Upper limit 9 1.697 2 0.921 9 2.113 5 1.405 6 4.132 0 37.764 1 1.354 8 2.536 7 10.809 7 6.562 8 7.502	Z-Value 7 -1.312 1 -2.179 8 -0.066 5 -1.355 2 5.789 4 1.611 6 0.116 9 0.482 2 1.159 9 0.540	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630 0.246 0.589	
Smoking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600 2.012 1.545 1.962	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237 2 0.617 5 0.318 2 0.935	2.637 Upper limit 9 1.697 2 0.921 9 2.113 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	Z-Value 7 -1.312 1 -2.179 8 -0.066 5 -1.355 2 5.789 1 1.611 6 0.116 0 0.482 2 1.159 2 0.540 3 1.781	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630 0.246 0.589 0.075	
Smoking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004 Sevuk, 2015	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600 2.012 1.545 1.962 0.748	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237 2 0.617 5 0.318 2 0.935 8 0.413	2.637 Upper limit 9 1.697 2 0.921 9 2.113 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	4.636 Z-Value 7 -1.312 1 -2.179 3 -0.066 5 -1.355 2 5.789 4 1.611 6 0.116 9 0.482 2 1.159 2 0.540 3 1.781 6 -0.958	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630 0.246 0.589 0.075 0.338	
Smoking current	Caldas, 2019 Chen, 2017 Dong, 2014 Kazmierski, 2014b Khan, 2014 Mardani, 2012 Martin, 2010 Norkeine, 2007 Omiya, 2015 Otomo, 2013 Rudolph, 2005 Santana Santos, 2004	0dds ratio 0.343 0.442 0.97- 0.467 2.886 8.358 1.147 1.053 1.600 2.012 1.545 1.962	1.482 Statis Lower limit 3 0.069 2 0.212 4 0.449 7 0.155 6 2.016 8 1.850 7 0.971 3 0.438 0 0.237 2 0.617 5 0.318 2 0.935 8 0.413 5 0.649	2.637 Upper limit 9 1.697 2 0.921 9 2.113 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	4.636 Z-Value 7 -1.312 1 -2.179 8 -0.066 5 -1.355 2 5.789 1 1.611 6 0.116 0 0.482 2 1.159 2 0.540 8 1.781 6 -0.958 8 0.395	p-Value 0.190 0.029 0.948 0.175 0.000 0.006 0.107 0.908 0.630 0.246 0.589 0.075 0.338 0.693	



Pre-Operative (Continuous)

Age (years) *	Study name			Statistics for	or each st	tudy			Difference in means and 95% CI	
	8 5 5 6 1 8	Difference in means	Standard error	Variance	Lower	Upper	Z-Value	p-Value		
	Caldas, 2019	5.000	2.825	6.893	-0.146	10.146	1.904	0.057	1 1 1 1 1	
	Ohen, 2017	1.700	1.423	2.025	-1.089	4.489	1.195	0.232		
	Leenders 2018	5,800	1.438	2.087	2.982	8.618	4.034	0.000		8
	Oldham, 2018	4.100	2.172	4.717	-0.157	8.357	1.888	0.059		
	Cumurou, 2008	4.780	3.531	12,470	-2.141	11.701	1.354	0.178		
	Dong, 2014	6.700	1.399	1.958	3.958	9.442	4.788	0.000		
	Eriksson, 2002	4.200	1.834	3.382	0.606	7.794	2.291	0.022		_
	Al Tmimi, 2016	2.749	2.177	4.739	-1.518	7.016	1.283	0.207		_
	Kazmierski, 2014a	6,666	1.442	2.079	3.840	9.492	4.623	0.000		-
	Khan, 2014	1.700	0.862	0.743	0.011	3.389	1.972	0.049		44.00
	Li, 2015	13.000	3.945	15.582	5.268	20.732	3.295	0.001		
	Loponen, 2008	6.200	2.163	4.679	1,980	10.440	2.866	0.004	_	_
	Mardani, 2012	-2.070	2.233	4.985	-6.446	2.308	-0.927	0.354		_
	Marispalco, 2012	5.000	0.997	0.995	3.045	6.955	5.013	0.000		_
	Mu. 2010	5.300	1.007	1.014	3.326	7.274	5.282	0.000		_
	Norkeine, 2007	5.800	1,434	2.056	2.990	8.610	4.045	0.000		-
	Oldham, 2015	5.600	2.543	6.465	0.617	10.583	2.202	0.028	 	72
	Otomo. 2013	1.000	1.815	3.295	-2.558	4.558	0.551	0.582		
	Palmbergen, 2012	7.520	1.318	1.736	4.937	10.103	5.707	0.000	1 1 1 L	-
	Plaschke, 2010	6.000	1.775	3.150	2.521	9.479	3.380	0.001	_	_
	Ringaitiene, 2015	2,500	2.875	8.264	-3.134	8.134	0.870	0.384		1
	Rudolph, 2009	8.600	1.715	2.942	5.238	11.952	5.014	0.000	- -	_
	Rudolph, 2006	2.200	1.365	1.863	-0.475	4.875	1.612	0.107	 = 	
	Santana Santos, 2004	2.880	0.785	0.616	1.342	4.418	3.669	0.000		
	Sevuk, 2015	-1.100	0.586	0.343	-2.249	0.049	-1.877	0.061	 	
	Siepe, 2011	6.200	3.816	14.563	-1.280	13.680	1.625	0.104		_
	Tully, 2010	2.500	1.819	3.307	-1.084	6.084	1,375	0.169	 	
	Zhang, 2015	2.610	1.287	1.657	0.087	5.133	2.028	0.043		
		4.144	0.610	0.372	2.948	5.339	6.792	0.000		
									-10.00 -5.00 0.00 5.00	

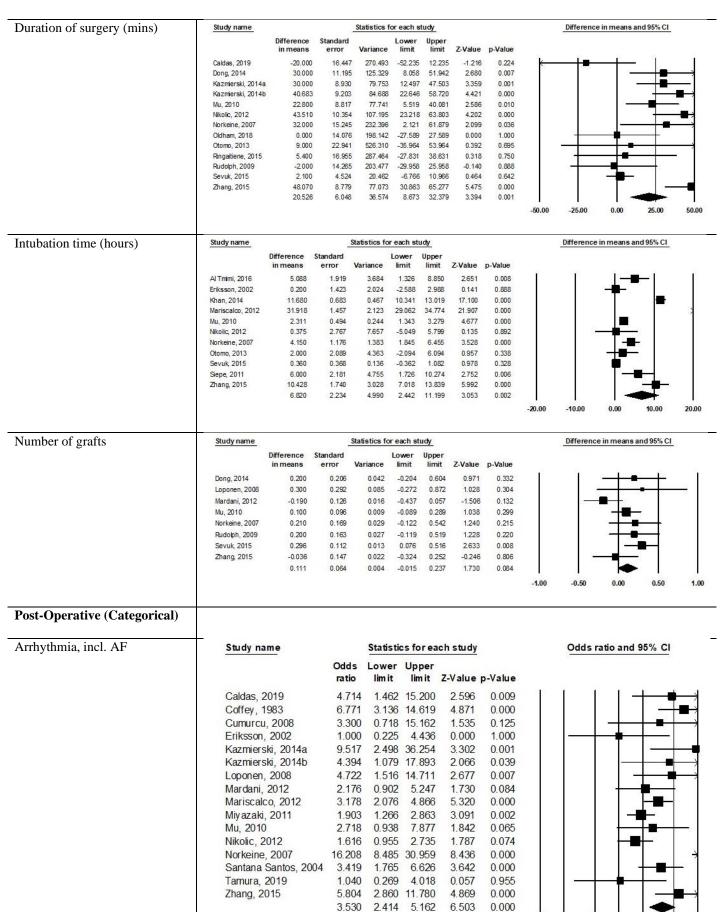
BMI	Study name			Statistics for	or each st	udy				Difference	e in means a	and 95% CI	
		Difference in means	Standard error	Variance	Lower	Upper limit	Z-Value	p-Value					
	Leenders, 2018	-0.700	0.637	0.405	-1.948	0.548	-1.100	0.272	1	1	-	- 1	- 1
	Dong, 2014	0.700	0.484	0.234	-0.249	1.649	1.446	0.148			-		
	Mu, 2010	-0.200	0.446	0.199	-1.074	0.674	-0.449	0.654			-		
	Norkeine, 2007	0.010	0.505	0.255	-0.980	1.000	0.020	0.984			-		
	Rudolph, 2009	0.300	1.505	2.264	-2.649	3.249	0.199	0.842			-		
	3000	0.026	0.249	0.062	-0.462	0.514	0.106	0.915			•	J	
									-10.00	-5.00	0.00	5.00	10.00

Cognition: All tests	Study name		5	tatistics for	eachst	udy				Sto	diff in mean	ns and 9	5% CI	
-	(a) (b)		Standard			Upper							S	
		in means					Z-Value p-			-	93		6 <u>0</u>	
	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		13				
	Al Tmimi, 2016	0.000	0.258	0.066	-0.505	0.505	0.000	1.000		-	-	8.6		
	Kazmierski, 2014a Li, 2015	-0.737 -0.912	0.202	0.041	-1.132 -1.821	-0.342 -0.004	-3.654 -1.968	0.000	198		- 38			
	Oldham, 2015	-0.784	0.293	0.215	-1.359	-0.210	-2.678	0.007	35.	10	- 28			
	Otomo, 2013	-0.772	0.268	0.072	-1.297	-0.210	-2.880	0.007						
	Rudolph, 2009	-0.572	0.248	0.061	-1.057	-0.086	-2.309	0.021		200	100 A			
	rtadajar, 2003	-0.576	0.105	0.011	-0.782	-0.370	-5.481	0.000						
									-2.00	-1.00	0.00	0).	1.00	2.
Constitute MMCE and														
Cognition: MMSE only	Study name	Difference	Standard	Statistics for	each st Lower	udy Upper				Differ	ence in me	eans ar	nd 95% CI	
		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	1 -	-	_ 1		- 1	
	Chen, 2017	-0.200	0.116	0.013	-0.428	0.028	-1.722	0.085						
	Oldham, 2018	-0.900	0.482	0.232	-1.845	0.045	-1.867	0.062			₽			
	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			<u>-</u>			
									-8.00	-4.00	0.0	0	4.00	8
Depression GDS	192000000000000000000000000000000000000			CVWs constants on	on the contract of	descention (Sec				Potoso	e 200 000 000 000 000 000 000 000 000 00			
Depression GDS	Study name	<u>Study name</u> <u>Statistics for each study</u> <u>Difference in means and 95% CI</u>												
		Difference	Standard		Lower									
		in means	error	Variance	limit	limi	t Z-Valu	e p-Value	•					
	Oldham, 2018	1.000	0.599	0.359	-0.17	4 2.1	74 1.66	69 0.09	5	1	200	1		-
		0.400	0.716	0.513	-1.00	14 1.8	04 0.55	59 0.576		- 1				
	Oldham 2015													
	Oldham, 2015									1	100			
	Oldham, 2015	0.753	0.459							1	10			-
	Oldham, 2015) -1.0	DO 0	.00	1.00	2.
Education (years)	Oldham, 2015				-0.14	8 1.6			1	M 194360	00 0	1000	001100	2.
Education (years)		0.753	0.459	0.211	-0.14	1.6	54 1.63		1	M 194360	0000	1000	001100	2.
Education (years)			0.459 Standan	0.211	-0.14	h study	54 1.63 mer	39 0.10	-2.00	M 194360	0000	1000	001100	2
Education (years)	Study name	0.753 Difference	0.459 Standar	0.211 Statistics Variance	-0.14 s for each	h study	54 1.63 mer nit Z-Val	39 0.10	-2.0i	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019	0.753 Difference in means -1.36	0.459 Standar error	Statistics Variance 34 2.83	-0.14 s for each Lower limit 7 -4.6	h study er Upp it lin	54 1.60 mer nit Z-Va i	ue p-Valu	1 -2.00 e 9 	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmerski, 2014c	0.753 Difference in means -1.36 -1.76	0.459 Standar error 1 1.6 1 0.5	0.211 Statistics Variance 4 Variance 4 0.30	-0.14 For each Lowe Imi -4.6 2 -2.8	h study er Upp it lim 363 1.9	ser nit Z-Val 940 -0.8	ue p-Valu 308 0.41 308 0.41 206 0.00	1 -2.00 e 9 1	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmerski, 2014b	0.753 Difference in means -1.36 -1.76 -1.22	0.459 Standar error 1 1.6 1 0.5 0 0.8	0.211 Statistics Variance 4 2.83 49 0.30 78 0.77	-0.14 s for eacl Lower in i	h study er Upp it lim 663 1.9	ser er Z-Val 940 -0.8 684 -3.2 502 -1.3	ue p-Valu 508 0.41 206 0.00 388 0.16	-2.04 e 9 	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015	0.753 Difference in means -1.36 -1.76 -1.22 1.30	0.459 Standar error 1 1.6 1 0.5 0 0.8 0 2.2	0.211 Statistics Variance 34 2.83 49 0.30 78 0.77 30 5.24	-0.14 Lowe limi 7	h study er Upp it lim 38 -0.038 -0.041 0.941 0.941	54 1.63 ber Z-Val 2-Val 684 -3.2 5502 -1.3 788 0.5	ue p-Valu 808 0.41 206 0.00 388 0.16 568 0.57	-2.00	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00	Standar error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5	0.211 Statistics Variance 34 2.83 49 0.30 78 0.77 60 5.24 58 0.31	-0.14 Lowe Imiliary -4.6 2	h study er Upppit lim 663 1.9 338 -0.9 441 0.9 488 5.1	54 1.63 Ser Z-Vali 940 -0.8684 -3.2. 502 -1.3. 788 0.5	ue p-Valu 808 0.41 206 0.00 388 0.16 668 0.57	-2.00	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00	Standar error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7	0.211 Statistics Variance 2.83 94 0.30 78 0.77 90 5.24 88 0.55	-0.14 Lower limit 7 -4.6 2 -2.8 2 -3.1 2 -1.0 9 -2.4	h study er Upppit lim it 338 -0.041 0.941	54 1.63 ber z-Val 940 -0.8684 -3.2 502 -1.3 788 0.5 094 0.0 466 -1.3	ue p-Valu 808 0.41 206 0.00 388 0.16 668 0.57 600 1.00	-2.00	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00	Standar error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7	0.211 Statistics Variance 2.83 94 0.30 78 0.77 90 5.24 88 0.55	-0.14 Lower limit 7 -4.6 2 -2.8 2 -3.1 2 -1.0 9 -2.4	h study er Upppit lim 663 1.9 338 -0.9 441 0.9 488 5.1	54 1.63 ber z-Val 940 -0.8684 -3.2 502 -1.3 788 0.5 094 0.0 466 -1.3	ue p-Valu 808 0.41 206 0.00 388 0.16 668 0.57 600 1.00	-2.00	M 194360	0000	1000	001100	2
Education (years)	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00	Standar error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7	0.211 Statistics Variance 2.83 94 0.30 78 0.77 90 5.24 88 0.55	-0.14 Lower limit 7 -4.6 2 -2.8 2 -3.1 2 -1.0 9 -2.4	h study er Upppit lim it 338 -0.041 0.941	54 1.63 ber z-Val 940 -0.8684 -3.2 502 -1.3 788 0.5 094 0.0 466 -1.3	ue p-Valu 808 0.41 206 0.00 388 0.16 668 0.57 600 1.00	-2.00	Diffe	rence in m	1000	001100	->
Education (years) EuroSCORE	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92	Standar error 1 1.66 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7 6 0.3	0.211 Statistics Variance 2.83 94 0.30 78 0.77 90 5.24 88 0.55	-0.14 Lower limit 17 -4.6 12 -2.8 12 -1.0 19 -2.4 17 -1.6 17 -1.6	h study Per Upppit lim 1683 1.9 438 -0.9 441 0.9 441 0.9 466 0.9 552 -0.9	54 1.63 ber z-Val 940 -0.8684 -3.2 502 -1.3 788 0.5 094 0.0 466 -1.3	ue p-Valu 808 0.41 206 0.00 388 0.16 668 0.57 600 1.00	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmerski, 2014b Li, 2015 Mu, 2010 Otomo, 2013	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00	Standar error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7	0.211 Statistics Variance 34 2.63 349 0.30 78 0.77 30 5.24 58 0.31 48 0.55 70 0.13	-0.14 Lower limit 7 -4.6 2 -2.8 2 -3.1 2 -1.6 9 -2.4 6 7 -1.6	h study Per Upppit lim 1683 1.9 438 -0.9 441 0.9 441 0.9 466 0.9 552 -0.9	54 1.63 ber z-Val 940 -0.8684 -3.2 502 -1.3 788 0.5 094 0.0 466 -1.3	ue p-Valu 808 0.41 206 0.00 568 0.57 700 1.0	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010 Otomo, 2013	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means	Standard error 1 1.6 1 0.5 0 0.8 0 0.7 6 0.3	0.211 Statistics 1	-0.14 Lower limit -0.14 Lower limit -0.14 Lower limit	h study Per Upper lim 1663 1.3 1.3 1.41 0.	Ner rait Z-Val 940 -0.8 684 -3.2 602 -1.3 788 -0.5 939 -0.1 2200 -2.4 Z-Value	ue p-Value p-Value p-Value p-Value p-Value	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmerski, 2014b Li, 2015 Mu, 2010 Otomo, 2013	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92	Standard error 1 1.6 1.0 0.8 0 0.8 0 0.7 0.0 0.7 6 0.3	0.211 Statistics Variance 4	-0.14 Lower limit -7 -4.6 -2 -2.8 -2 -3.1 -1.0 -1.6 reach st	h study er Upp it lim 363 1.9 441 0.9 441 0.9 488 5.1 944 1.4 666 0.4 552 -0.	Ner riit Z-Val 940 -0.8884 -3.2502 -1.3788 0.5994 0.466 -1.3200 -2.4	ue p-Valu 808 0.41 206 0.00 568 0.57 700 1.0	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmerski, 2014c Kazmerski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name	0.753 Difference in means -1.36 -1.76 -1.22 1.30 -1.00 -1.00 -1.00 -1.00 -1.00 -0.92	0.459 Standard error 1	0.211 Statistics 1	-0.14 s for each si for each	18 1.6 h study h study Upper imit 0.791	Ser T-Val 1.6: 2-Val 1	ue p-Value 808 0.41 206 0.00 388 0.16 668 0.57 0.00 1.00 337 0.18 499 0.01	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmerski, 2014c Kazmerski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992	Standard error 1 1.6 1 0.5 0 0.8 0 2.2 0 0.5 0 0.7 6 0.3	0.211 Statistics d Variance 0.061 0.426 0.061 0.426 0.061 0.426 0.211 0.061 0.426 0.021 0.021 0.061 0.426 0.021	-0.144 b for each lower limit 7	8 1.6 study h study lim lim lim lim lim lim lim lim lim li	ser rit Z-Val	ue p-Value 808 0.41 206 0.00 838 0.16 668 0.57 1.00 0.01 p-Value 0.218 0.128	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dong, 2014	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500	Standard error 1 1.6.1 1 0.5.5 0 0.8 0 2.22 0 0.5.6 0 0.7 6 0.3	0.211 Statistics Variance 0.061 0.428 0.039	-0.14 Lower limi -0.16 -0.14 Lower limi -0.180 -0.180 -0.180 -0.180 -0.180 -0.180 -0.180 -0.180 -0.111	18 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1	Ever init Z-Valia 2-Valia 3-1,521 2.519	ue p-Value 0.410 0.00 0.410 0.00 0.10 0.10 0.337 0.18 0.99 0.01	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dang, 2014 Loponen, 2008	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500 1.800	Standard error 1 1.6 1 0.5 0 0.8 0 0.7 1 0.5 0 0.5 0 0.7 1 0 0.5 0 0 0.5 0 0 0.7 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.211 Statistics 1	-0.144 Lower limit -0.186 -0.194 Lower limit -0.180 -0.286 -0.111 -0.280	18 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1	Evalue 1.233 1.521 2.335	ue p-Value 0.218 0.102 0.218 0.102 0.020	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	
	Study name Caldas, 2019 Kazmerski, 2014c Kazmerski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dong, 2014 Loponen, 2008 Marsin, 2012	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500 1.800 5.600	Standard error 1	0.211 Statistics 1	-0.144 s for each state Lower limit -0.180 -0.286	18 1.6 study Wuper limit 0.791 2.271 0.899 3.311 6.467	Ser viit Z-Val 940 -0.8 684 -3.4 502 -1.3 7788 0.5 094 0.0 486 -1.3 200 -2.4 Z-Value 1.233 1.521 2.538 12.864	ue p-Value 0.410 0.57 0.600 0.000 0.000 0.000 0.000 0.000 0.000	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dong, 2014 Loponen, 2008 Marsin, 2012 Mu, 2010 Norkeine, 2007 Ringaitiene, 2015	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500 1.800 5.600 1.200 1.700 0.000	Standard error 1	Statistics of Variance 0.241 Statistics of Variance 0.048 0.039 0.594 0.198 0.063 0.143 0.294	-0.144 Example 10 -0.144 Example 10 -0.144 Example 10 -0.144 Example 11 -0.144 Example 12 -0.144 Examp	18 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1	Evalue 1.63 Evalue 1.233 1.521 2.519 2.335 12.664 4.77 4.489 0.000	39 0.10 ue p-Valu 308 0.41 206 0.00 338 0.16 368 0.57 100 1.000 p-Value 0.218 0.128 0.012 0.020 0.000 0.000 1.000	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014c Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dong, 2014 Loponen, 2008 Marsin, 2012 Mu, 2010 Norkeine, 2007 Ringuiliene, 2015 Sevuk, 2015	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500 1.800 1.200 1.200 0.000 0.010	Standard error 1	Statistics 1	-0.144 s for each state Lower limit -0.160 -0.286	18 1.6 1.6 1.6 1.6 1.6 1.6 1.6 1.6 1.6 1.6	Errit Z-Val 940 -0.8 884 -3.4 502 -1.3 788 0.5 7994 0.6 466 -1.3 200 -2.4 Z-Value 1.233 1.521 2.519 2.335 12.664 4.777 4.490 0.236	ue p-Value 0.410 0.57 0.001 0.001 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.001	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	->
	Study name Caldas, 2019 Kazmierski, 2014c Kazmierski, 2014b Li, 2015 Mu, 2010 Otomo, 2013 Study name Al Tmimi, 2016 Caldas, 2019 Dong, 2014 Loponen, 2008 Marsin, 2012 Mu, 2010 Norkeine, 2007 Ringaitiene, 2015	0.753 Difference in means -1.36 -1.76 -1.22 1.30 0.00 -1.00 -0.92 Difference in means 0.305 0.992 0.500 1.800 5.600 1.200 1.700 0.000	Standard error 1	Statistics of Variance 0.241 Statistics of Variance 0.048 0.039 0.594 0.198 0.063 0.143 0.294	-0.144 Example 10 -0.144 Example 10 -0.144 Example 10 -0.144 Example 11 -0.144 Example 12 -0.144 Examp	18 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1.8 1	Evalue 1.63 Evalue 1.233 1.521 2.519 2.335 12.664 4.77 4.489 0.000	39 0.10 ue p-Valu 308 0.41 206 0.00 338 0.16 368 0.57 100 1.000 p-Value 0.218 0.128 0.012 0.020 0.000 0.000 1.000	-2.00	<u>Diffe</u>	rence in m	neans ai	2.00	4.4

Intra-Operative (Continuous)

ACC time (mins)	Study name		1	Statistics fo	reach s	tudy				Difference	in means	and 95% CI	
, ,		Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
	Caldas, 2019	-13.000	6.766	45.776	-26.261	0.261	-1.921	0.055	k-	-	-	i i	
	Leenders, 2018	6.100	2.598	6.749	1.008	11.192	2.348	0.019	1	20000	- 1		
	Cumurcu, 2008	18.940	8.191	67.093	2.886	34.994	2.312	0.021			_		-
	Eriksson, 2002	4.300	5.280	27.879	-6.049	14.649	0.814	0.415		-	_		
	Kazmierski, 2014a	4.012	2.586	6.687	-1.056	9.081	1.552	0.121			-		
	Kazmierski, 2014b	5.534	2.703	7.307	0.236	10.832	2.047	0.041			-		
	Khan, 2014	28.220	2.004	4.017	24.292	32.148	14.081	0.000				*****	
	Loponen, 2008	8.000	6.821	46.528	-5.369	21.369	1.173	0.241		8=	25-20		_
	Mardani, 2012	2.000	2.182	4.760	-2.276	6.276	0.917	0.359				_	
	Mariscalco, 2012	19.800	3.501	12.260	12.937	26.663	5.655	0.000			-02	122-	_
	Nikolic, 2012	1.177	2.456	6.032	-3.637	5.991	0.479	0.632				_	
	Norkeine, 2007	3.100	3.378	11.414	-3.522	9.722	0.918	0.359					
	Ringaitiene, 2015	-5.500	6.913	47.789	-19.049	8.049	-0.796	0.426	90				
	Santana Santos, 2004	2.040	3.579	12.810	-4.975	9.055	0.570	0.569					
	Sevuk, 2015	-0.733	3.151	9.930	-6.910	5.443	-0.233	0.816	- 1		_		
	Tully, 2010	8.100	3.994	15.956	0.271	15.929	2.028	0.043					-():
	24(1)	5.970	2.732	7.462	0.616	11.324	2.185	0.029	- 1				

CPB time (mins)	Study name			Statistics f	or each st	udy				Difference	e in means a	nd 95% CI	
, ,		Difference in means	Standard error	Variance	Lower	Upper limit	Z-Value	p-Value					
	Caldas, 2019	-7.000	7.876	62.035	-22.437	8.437	-0.889	0.374	1	\rightarrow	-	-3 1	
	Cumuray, 2008	15.260	8.490	72.077	-1.380	31.900	1.797	0.072			-	-	_
	Erikson, 2002	8.900	9.834	98.701	-10.374	28.174	0.905	0.365				•	_
	Gottesman, 2010	5.100	1.922	3.695	1.333	8.867	2.653	0.008					
	Kazmierski, 2014a	12.660	3.839	14.740	5.135	20.184	3.297	0.001		- 1	15	-	
	Kazmierski, 2014b	15.349	4.988	24.883	5.615	25.082	3.091	0.002		- 1	- 1		_
	Khan, 2014	2.100	3.316	10.995	-4.399	8.599	0.633	0.527		- 1	_	-	
	Leenders, 2018	0.764	5.346	28.576	-9.713	11.241	0.143	0.886		-		_ l	
	Li. 2015	46.200	45.417	2082.711	-42.816	135.218	1.017	0.309	-	_	-	_	_
	Loponen, 2008	10.000	7.903	82.482	-5.490	25.490	1.265	0.208	1000	1	-		_
	Mardani, 2012	2.000	3.442	11.847	-4.748	8.746	0.581	0.561		- 1			
	Marisoaloo, 2012	25.700	4.450	19.799	16,979	34.421	5.776	0.000		- 1		_	_
	Nikolic, 2012	9.073	3.045	9.272	3.105	15.041	2.980	0.003		- 1	S-	-	
	Norkeine, 2007	11.800	6.069	36.837	-0.096	23,696	1.944	0.052		- 1	\vdash		_
	Oldham, 2018	-3.000	9.730	94.881	-22.071	16.071	-0.308	0.758				-	
	Otomo, 2013	21.000	16.018	256.565	-10.394	52.394	1.311	0.190		· -	1723		-
	Ringaitene, 2015	-0.100	10.799	118.611	-21,285	21.085	-0.009	0.993		_	-	-	
	Rudolph, 2009	2.000	6.794	46.158	-11.316	15.316	0.294	0.768		-		_	
	Santana Santos 2004	3.970	5.280	27.873	-6.378	14.318	0.752	0.452		- 1			
	Sewk, 2015	0.282	4.949	24.492	-9.418	9.982	0.057	0.955	- 1	<u></u>		_	
	Siepe, 2011	20.000	11.678	136.385	-2.889	42.889	1.713	0.087	- 1	- 1	-		
		7.406	1.724	2.972	4.027	10.784	4.296	0.000			4	-	
									-30.00	-15.00	0.00	15.00	



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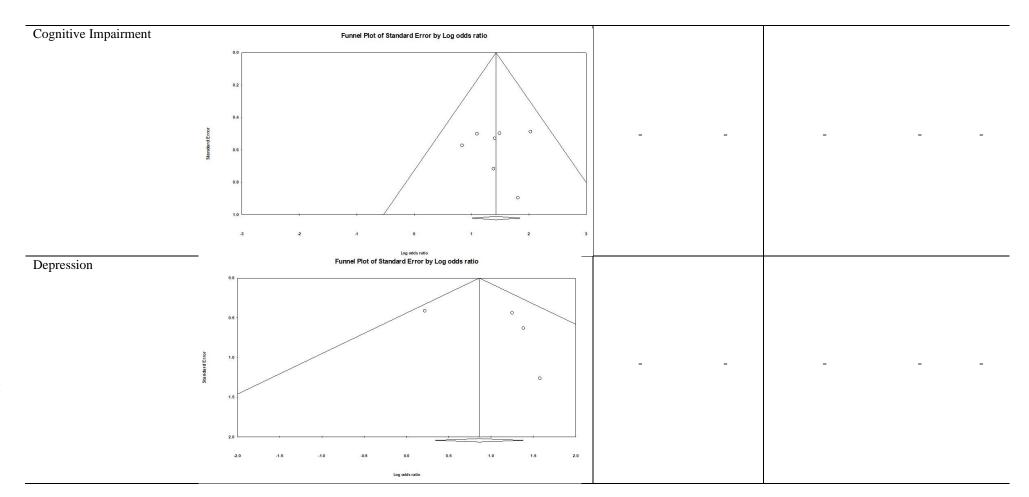
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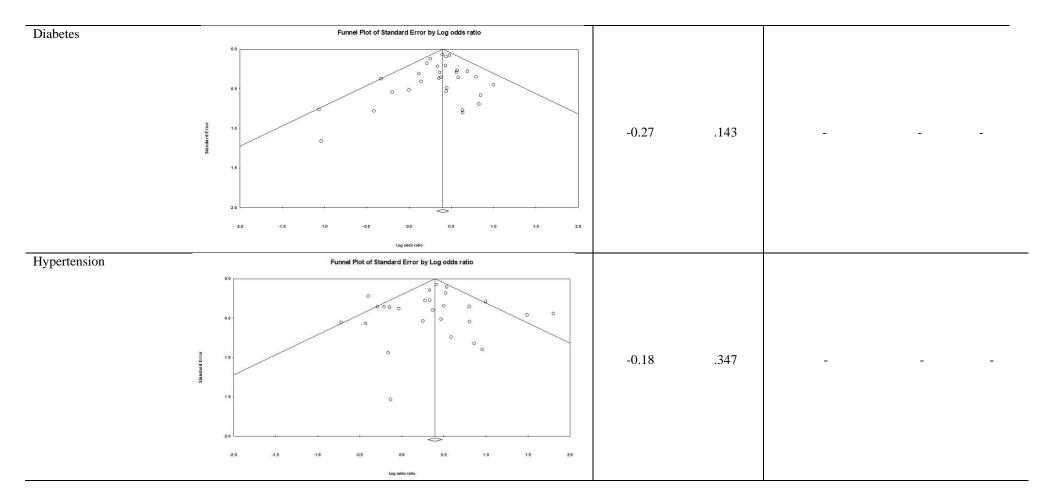
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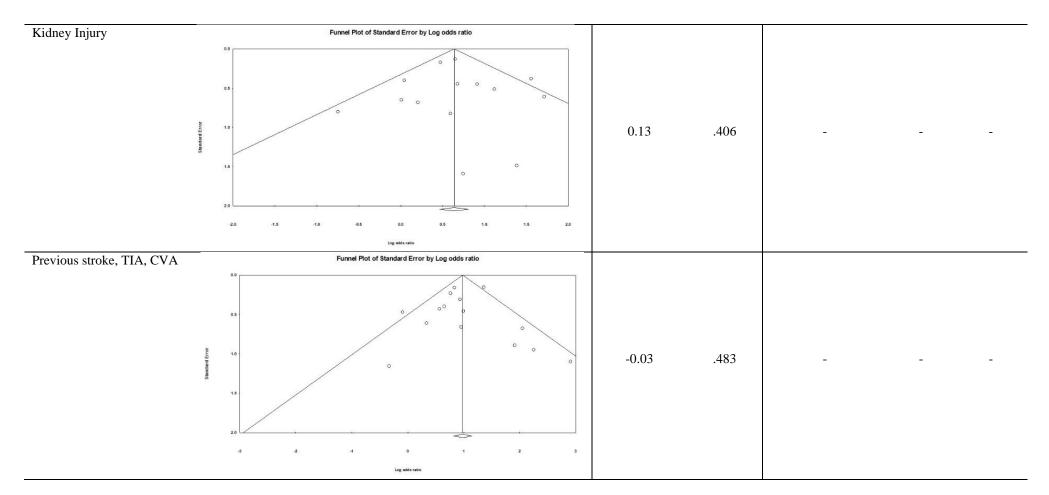
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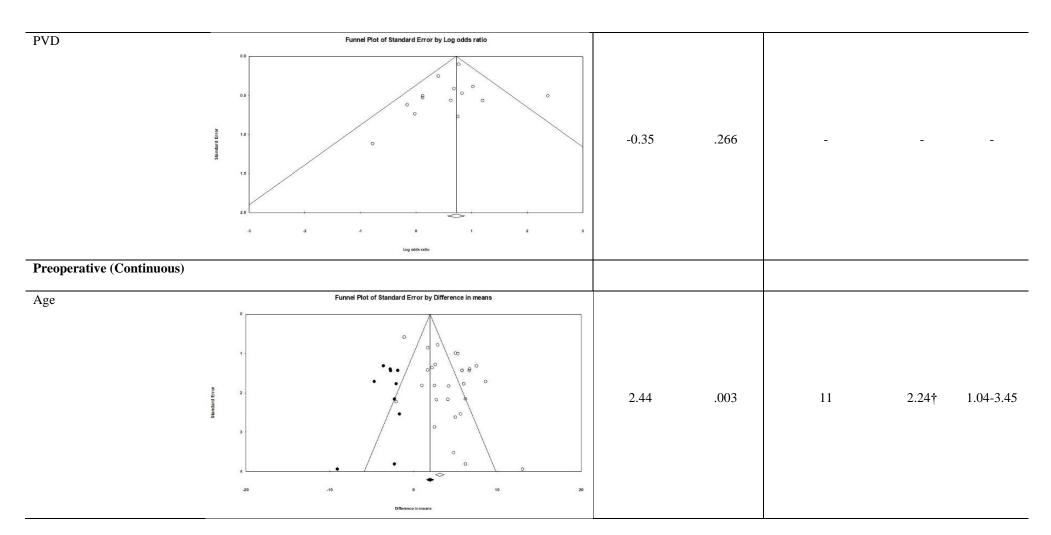
rative (Continuous)													
U (days)	Study name			Statistics fo	or each st	tudy				Differenc	e in means	and 95% CI	
		Difference in means	Standard error	Variance	Lower	Upper limit	Z-Value	p-Value					
	Al Tmimi, 2016	1.491	0.339	0.115	0.826	2.155	4.396	0.000	1	Î	1 4	- 1	
	Caldas, 2019	2.910	1.833	3.361	-0.683	6.503	1.587	0.112		- 1	-	-	- 8
i d	Chen, 2017	2.253	0.272	0.074	1.721	2.786	8.295	0.000		- 1		-	
E	Eriksson, 2002	-0.100	0.209	0.044	-0.509	0.309	-0.479	0.632		- 1			
1	Chan, 2014	6.510	0.234	0.055	6.052	6.968	27.852	0.000		- 1	100		
1	Mardani, 2012	0.530	0.251	0.063	0.037	1.023	2108	0.035		- 1		100-001	
1	Mariscalco, 2012	2.188	0.074	0.005	2.043	2.333	29.630	0.000		- 1	200-0		
1	Mu, 2010	0.920	0.197	0.039	0.533	1.306	4.666	0.000		- 1	=	3	
1	Norkeine, 2007	4.800	0.438	0.191	3.943	5.657	10.971	0.000		- 1	1		
	Omiya, 2015	1.385	0.349	0.122	0.701	2.070	3.965	0.000		- 1	17 2	-	
F	Palmbergen, 2012	2.990	0.385	0.148	2.236	3.744	7.773	0.000		- 1		-	
	Siepe, 2011	1.500	1.381	1.906	-1.206	4.206	1.087	0.277		- 1	8	-	
	Subramaniam, 2019	1.412	0.353	0.125	0.720	2.105	3.996	0.000		- 1	100	-	
	Zhang, 2015	2.500	0.311	0.097	1.890	3.110	8.035	0.000				-	
		2.221	0.462	0.213	1.316	3.126	4.812	0.000		13	989	•	
									-6.00	-3.00	0.00	3.00	6
										0.00			
									-6.00	-3.00		0.00	0.00 3.00

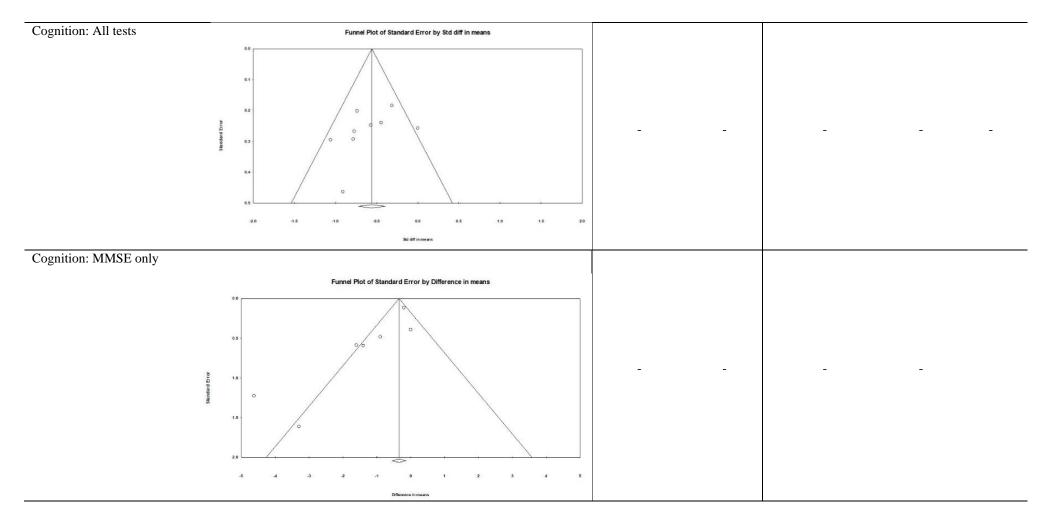
Figure S2. Funnel plo	ets for statistically significant analyses in regard to delirium	Egger'	s Test	Tri	m and Fill	
	lts of publication bias/small-study effect investigation when	Intercept	p value (1-tailed)	No. imputed studies	OR/MD† /SMD‡	95%CI
Preoperative (Categorical						
Arrhythmia, incl. AF	Funnel Plot of Standard Error by Log odds ratio	-0.08	.432	-	-	-
BMI ≥30 only	Punnel Plot of Standard Error by Log odds ratio	-	-	-	-	-



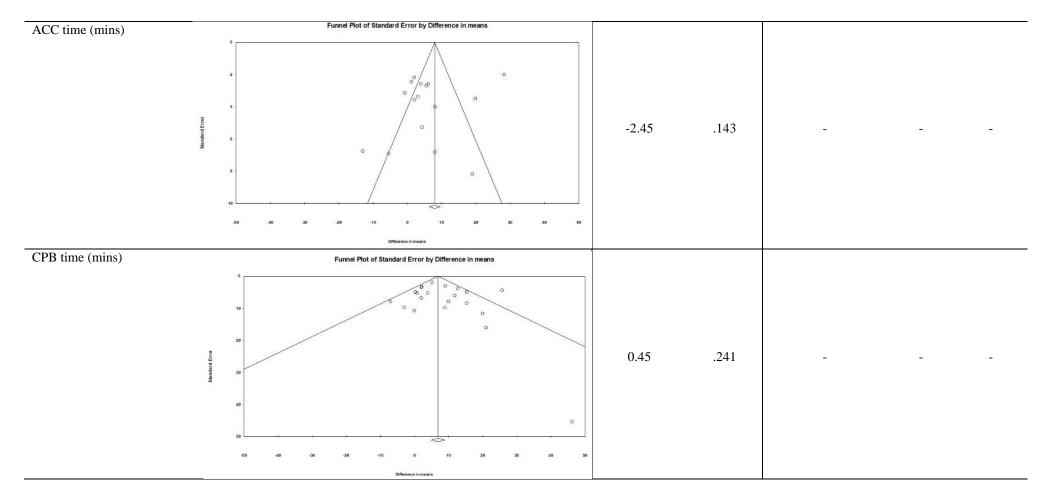




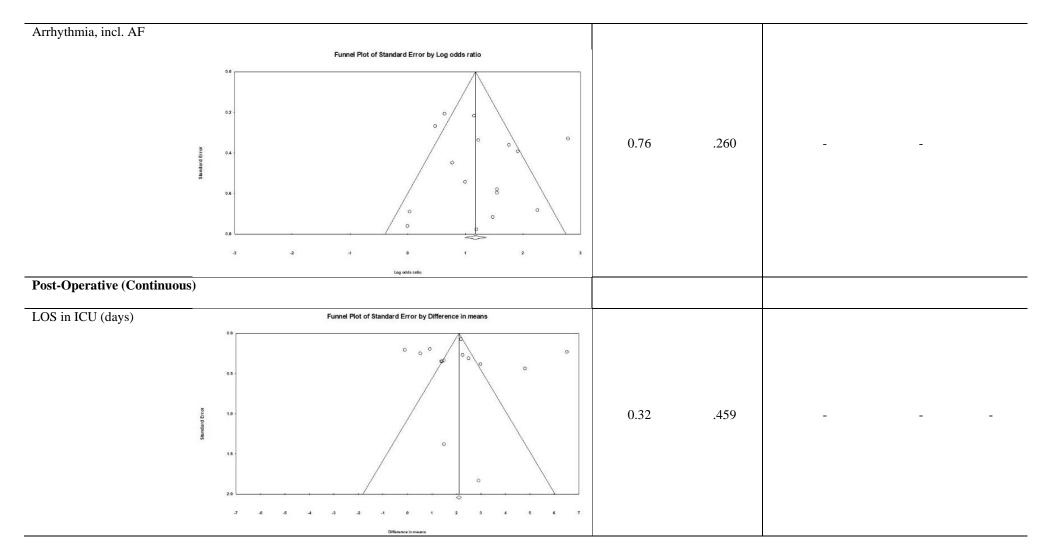




Education (years)	Funnel Plot of Standard Error by Difference in means		
	20 15 19 45 60 05 19 15 20		-
EuroSCORE	Funnel Plot of Standard Error by Difference in means		
	0.6 0.6 0.6 0.6 0.6 0.6 0.6 0.6 0.6 0.6	4.36 .010	5 0.15† -0.60-0.90
	Ofference in means		
Intra-Operative (Contin	nuous)		



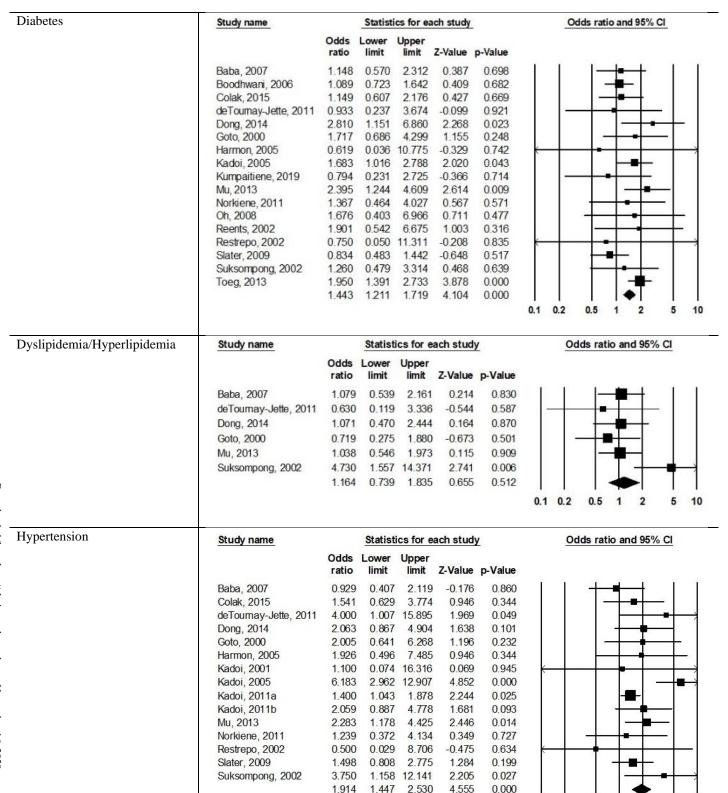
Duration of surgery (mins)	Funnel Plot of Sta	andard Error by Difference in means				
	Sampling Erica	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.77	.296	-	
	-30 -40 -30 -20 -10	Difference in means				
Intubation time (hours)	Funnel Plot of Star	ndard Error by Difference in means				
	2 Sandaria Erica 2 - 20 40 30 20 10	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	5.20	.106	-	-



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Figure S3. Forest 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			Odds ra	atio a	nd 95%	CI	
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value						
	Colak, 2015	11.000	1.425	84.927	2.299	0.021	1 1	T	1	+	-	_
	Dong, 2014	1.459	0.561	3.795		0.439	- 1 - 1	١,	\rightarrow	•	-	
	Mu, 2013	0.938	0.397	2.214	-0.147	0.883	- 1 - 1	+		=		
	Norkiene, 2011	1.170	0.356	3.843	0.258	0.796	- 1 - 1	-		-	-	
	Restrepo, 2002	0.905	0.029	27.858	-0.057	0.954	k		-	(e)	_	->
	Slater, 2009	0.495	0.056	4.360	-0.634	0.526	 	+	+	-	-	
	Suksompong, 2002	1.090	0.216	5.504	0.104	0.917		-	-		\rightarrow	
	W	1.243	0.757	2.041	0.861	0.389			+			
							0.1 0.3	2 0.8	1	2	5	10
Cognitive Impairment	Study name		Statistic	s for e	ach stud	ly	9	Odds r	atio	and 95	% CI	
		Odds L ratio	ower limit		Z-Value	p-Value						
	Baba, 2007	0.752	0.161	3.504	-0.363	0.717	-	1			- Î	1
	Control of the Contro	1.241	0.463	3.329	0.430					-0)	<u></u>	
		0.898	0.455	1.774	-0.309			_		_		
	Trubnikova, 2014		0.680	3.654	1.060							
		1.108	0.709	1.730	0.449					-		
							0.1 0	.2 0	5 1	2	5	10
Depression	Study name	Sta	itistics	for eac	h study	9	0	dds ra	tio a	nd 95	% CI	
	Odd	ds Lov	ver Up	per								
	rat				-Value	p-Value						
	Kadoi, 2011b 6.2	17 2.	199 17	.580	3.446	0.001				1-	-	\blacksquare
	Slater, 2009 1.9	85 0.	791 4	.980	1.461	0.144			_			
	3.4		119 10		2.157	0.031				$-\Box$		-
							0.1 0.	2 0.	5 1	2	5	10



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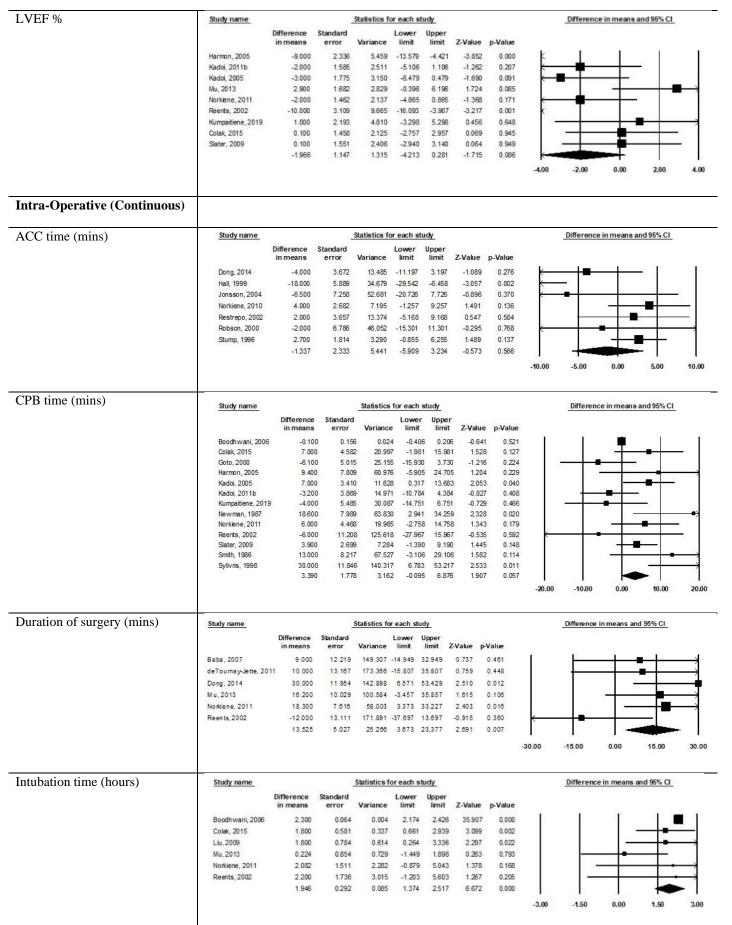
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Sex (male)	Study name		Statis	tics for e	ach study		Odds ratio and 95% CI
		Odds ratio	Lower	Upper limit	Z-Value	p-Value	
	Baba, 2007	0.972	0.459	2.060	-0.074	0.941	
	Boodhwani, 2006	1.206	0.692	2.102	0.660	0.509	
	Christiansen, 2016	1.667		58.281	0.282	0.778	K
	Colak, 2015 deTournay-Jette, 201	1.322			0.772 -0.665	0.440	
	Dong, 2014	0.811			-0.665	0.662	
	Goto, 2000	1.324			0.548	0.584	
	Hall, 1999	0.574		2.810		0.494	
	Harmon, 2005	0.750			-0.305	0.760	
	Kadoi, 2005 Kadoi, 2011b	0.896			-0.292 -0.490	0.770	
	Kumpaitiene, 2019	1.488			0.719	0.624	
	Mu, 2013	0.988				0.979	++
	Norkiene, 2011	1.270	0.517		0.522	0.602	
	Reents, 2002	1.037			0.039	0.969	
	Restrepo, 2002	3.267		82.036	0.720	0.472	
	Slater, 2009 Suksompong, 2002	0.795			-0.625 -0.159	0.532	
	ounsumpung, 2002	1.026			0.223	0.824	
		117.70				3657.1	0.1 0.2 0.5 1 2 5 10
Kidney injury	Study name		Statist	ics for ea	ach study	,	Odds ratio and 95% CI
J . J J			Lower	Upper			,),
	10. P. V. 1 100 100 100 100 100 100 100 100 100	ratio	limit	limit		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	-1.409	0.159	
	Suksompong, 2002	4.200	1.018	17.327	1.985	0.047	
		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		Statistic	ce for ea	ch study		Odds ratio and 95% CI
revious ivii	88	Odds	Lower		cii study		Odds ratio and 35 % Cr
		ratio				n Value	
		Tauo	limit	limit	Z-Value	p-value	
	Colak, 2015	1.155	0.376	3.552	2-Value 0.252	0.801	
						WANTED THE COLUMN	
	Colak, 2015 Norkiene, 2011	1.155	0.376	3.552	0.252	0.801	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	1.155 1.621 0.750	0.376 0.528 0.240	3.552 4.975 2.342	0.252 0.844 -0.495	0.801 0.399 0.620	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	1.155 1.621	0.376 0.528	3.552 4.975	0.252 0.844	0.801 0.399	
	Colak, 2015 Norkiene, 2011 Suksompong, 2002	1.155 1.621 0.750	0.376 0.528 0.240	3.552 4.975 2.342	0.252 0.844 -0.495	0.801 0.399 0.620	0.1 0.2 0.5 1 2 5 10
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002	1.155 1.621 0.750	0.376 0.528 0.240 0.586	3.552 4.975 2.342 2.156	0.252 0.844 -0.495	0.801 0.399 0.620 0.724	0.1 0.2 0.5 1 2 5 10 Odds ratio and 95% CI
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name	1.155 1.621 0.750 1.124	0.376 0.528 0.240 0.586 Statisti	3.552 4.975 2.342 2.156	0.252 0.844 -0.495 0.353	0.801 0.399 0.620 0.724	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name	1.155 1.621 0.750 1.124	0.376 0.528 0.240 0.586	3.552 4.975 2.342 2.156	0.252 0.844 -0.495 0.353	0.801 0.399 0.620 0.724	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014	1.155 1.621 0.750 1.124	0.376 0.528 0.240 0.586 Statisti	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431	0.801 0.399 0.620 0.724 p-Value 0.152	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005	1.155 1.621 0.750 1.124 Odds ratio	0.376 0.528 0.240 0.586 Statisti	3.552 4.975 2.342 2.156 cs for ea	0.252 0.844 -0.495 0.353 ach study	0.801 0.399 0.620 0.724	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014	1.155 1.621 0.750 1.124 Odds ratio 1.831	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431	0.801 0.399 0.620 0.724 p-Value 0.152	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005	1.155 1.621 0.750 1.124 Odds ratio 1.831 1.246	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311	0.801 0.399 0.620 0.724 p-Value 0.152 0.755	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009	1.155 1.621 0.750 1.124 Odds ratio 1.831 1.246 1.776	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127	0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013	1.155 1.621 0.750 1.124 Odds ratio 1.831 1.246 1.776 0.698	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127 -1.103	0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011	1.155 1.621 0.750 1.124 Odds ratio 1.831 1.246 1.776 0.698 0.719	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354	3.552 4.975 2.342 2.156 cs for ea Upper limit 4.191 4.977 3.015 1.322 1.458	0.252 0.844 -0.495 0.353 ach study Z-Value 1.431 0.311 2.127 -1.103 -0.915	0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360	
Previous MI history/ever	Colak, 2015 Norkiene, 2011 Suksompong, 2002 Study name Dong, 2014 Harmon, 2005 Liu, 2009 Mu, 2013 Norkiene, 2011 Slater, 2009	1.155 1.621 0.750 1.124 Odds ratio 1.831 1.246 1.776 0.698 0.719 1.345	0.376 0.528 0.240 0.586 Statisti Lower limit 0.800 0.312 1.046 0.369 0.354 0.590	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	0.252 0.844 -0.495 0.353 Example 1.431 0.311 2.127 -1.103 -0.915 0.705	0.801 0.399 0.620 0.724 p-Value 0.152 0.755 0.033 0.270 0.360 0.481	

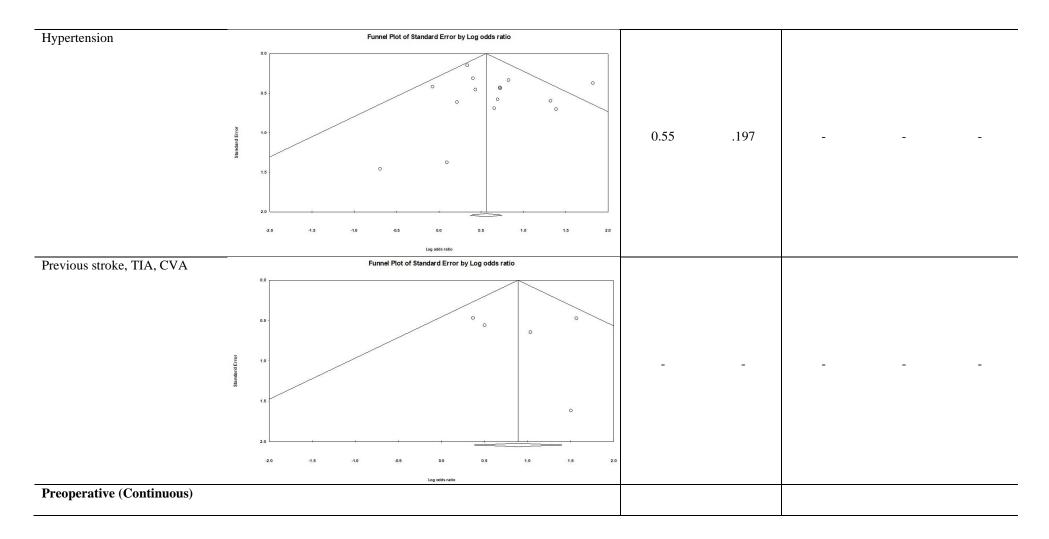
Previous stroke, TIA, CVA	Study name		Statisti	cs for ea	ch study	!	Odds ratio and 95% CI
		Odds ratio	Lower limit		Z-Value	p-Value	
	Baba, 2007	4.799	1.899	12.129	3.315	0.001	
	Dong, 2014	2.814	0.795	9.959	1.604	0.109	
	Mu, 2013	1.445	0.576	3.623	0.785	0.433	
	Restrepo, 2002			106.823	0.931	0.352	
	Slater, 2009	1.652		4.938	0.899	0.369	
	Clutci, 2000	2.435	1.468	4.038	3.447	0.001	
		2.400	1.400	4.050	5.447	0.001	
							0.1 0.2 0.5 1 2 5 10
PVD	Study name		Statis	tics for e	ach stud	У	Odds ratio and 95% CI
		Odds	Lower		Z-Value	p-Value	
	Baba, 2007	0.41				-	
	Boodhwani, 200						-
	Goto, 2000			1.748			
	Section of the property of the first of the	4.35					
	Restrepo, 2002	0.48		12.929			
		1.08	0.417	2.631	0.170	0.865	
							0.1 0.2 0.5 1 2 5 10
Smoking current/history	Study name		Statist	ics for e	ach stud	У	Odds ratio and 95% CI
	329	Odds ratio	Lower limit	Upper limit		p-Value	
	Daha 2007						
	Baba, 2007	0.902					
	Dong, 2014 Kadoi, 2001	0.10					
	Kadoi, 2001	1.03					T _ _
	Liu, 2009	0.33					│ │ ■↓ ▼ │ │ │
	Mu, 2013	1.382					· │ │ ─ │ │ ■┼ │ │
	Norkiene, 2011			3.798			
	Restrepo, 2002	2 15.000	0.597	376.696	1.647	0.100	
	Slater, 2009	1.729	0.997	2.99	7 1.950	0.051	
		1.033	0.642	1.664	0.135	0.892	
							0.1 0.2 0.5 1 2 5 10
Pre-Operative (Continuous)							
Age (years)	Study name	ference S	Statist	cs for each str	udy Upper		Difference in means and 95% CI
	1,770	means	error Varia	nce limit	limit Z-Value		
	1920 (200-2000)		0.987 0	973 -1.234	2.834 0.710		
	Baba, 2007 Boodhwani, 2006	0.700	0.038 0	001 0.425	0.575 13.00	5 0.000	- 10 COS 8
	Boodhwani, 2006 Christiansen, 2016	0.500 1.900	10.530 110	.882 -18,739	22.539 0.180	0.857	- - -
	Boodhwani, 2006 Christiansen, 2016 Colak, 2015 deTournay-Jette, 2011	0.500 1.900 7.300 -3.010	10.530 110 1.091 1 1.539 2	.882 -18.739 191 5.161 368 -6.026	22.539 0.180 9.439 6.680 0.006 -1.956	0 0.857 9 0.000 8 0.050	
	Boodhwani, 2008 Christiansen, 2016 Colak, 2015	0.500 1.900 7.300	10.530 110 1.091 1 1.539 2 1.526 2	.882 -18.739 191 5.161	22.539 0.180 9.439 6.685	0 0.857 9 0.000 8 0.050 1 0.000	
	Boodhwani, 2006 Chistianen, 2016 Colek, 2015 deTournay-Jette, 2011 Dong, 2014 Go to, 2000 Hall, 1999	0.500 1.900 7.300 -3.010 6.000 1.500 3.300	10.530 110 1.091 1 1.539 2 1.526 2 1.168 1 3.234 10	882 -18,739 191 5.161 368 -6.026 330 3.008 364 -0.789 460 -3.039	22.539 0.180 9.439 6.683 0.006 -1.956 8.992 3.93 3.789 1.284 9.639 1.020	0 0.857 9 0.000 5 0.050 1 0.000 4 0.199 0 0.308	
	Boodhwani, 2008 Chistianeen, 2016 Colak, 2015 deTournay-lette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Hamoon, 2005 Kadoi, 2005	0.500 1.900 7.300 -3.010 6.000 1.500 3.300 8.300 7.000	10.530 110 1.091 1 1.539 2 1.526 2 1.188 1 3.234 10 2.425 5 1.500 2	.882 -18.739 191 5.161 368 -6.026 330 3.008 364 -0.789 .460 -3.039 883 3.546 251 4.060	22.539 0.18 9.439 6.68 0.006 -1.95 8.992 3.93 3.789 1.28 9.639 1.020 13.054 3.422 9.940 4.686	0 0.857 9 0.000 5 0.050 1 0.000 4 0.199 0 0.308 2 0.001 5 0.000	
	Boodhwani, 2008 Chistianeen, 2016 Colak, 2015 deTournay-Jette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Hamoon, 2005	0.500 1.900 7.300 -3.010 6.000 1.500 3.300 8.300	10.530 110 1.091 1 1.539 2 1.526 2 1.168 1 3.234 10 2.425 5 1.500 2 1.098 1	.882 -18.739 191 5.161 368 -6.026 330 3.008 364 -0.789 .460 -3.039 883 3.546	22.539 0.180 9.439 6.683 0.006 -1.956 8.992 3.93 3.789 1.284 9.639 1.020 13.054 3.422	0 0.857 0 0.000 3 0.050 1 0.000 4 0.199 0 0.308 2 0.001 5 0.000 2 0.855	
	Boodhwani, 2008 Chistiansen, 2016 Colak, 2015 deTournay-lette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Hamoon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiene, 2019 Liu, 2009	0.500 1.900 7.300 -3.010 6.000 1.500 3.300 8.300 7.000 -0.200 4.000 2.000	10.530 110 1.091 1 1.539 2 1.528 2 1.168 1 3.234 10 2.425 5 1.500 2 1.098 1 2.176 4 1.117 1	.882 -18.739 191 5.161 368 -6.026 330 3.008 364 -0.789 .460 -3.039 .883 3.546 251 4.000 206 -2.352 .736 -0.265 247 -0.188	22.539 0.18(9.439 6.683 0.006 -1.95(8.992 3.93 3.789 1.28 9.639 1.02(13.054 3.42:49.940 4.66(1.952 -1.83) 4.188 1.79(1.952 -1.83)	0 0.857 9 0.000 5 0.050 1 0.000 4 0.199 0 0.308 2 0.001 5 0.000 2 0.855 8 0.086 1 0.073	
	Boodhwani, 2008 Chistiansen, 2016 Colak, 2015 deTournay-Jette, 2011 Dong, 2014 Go to, 2000 Hall, 1999 Hammon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiane, 2019 Liu, 2009 Mu, 2013 Newman, 1987	0.500 1.900 7.300 -3.010 6.000 1.500 3.300 8.300 7.000 -0.200 4.000 2.000 6.800	10.530 110 1.091 1 1.539 2 1.529 2 1.168 1 3.234 10 2.425 5 1.500 2 1.098 1 2.176 4 1.117 1 1.413 1 2.045 4	.882 -18.739 191 5.161 368 -6.026 330 3.008 364 -0.789 460 -3.039 883 3.546 251 4.000 206 -2.352 736 -0.265 736 -0.265 737 -0.188 996 -0.769 180 2.793	22.539 0.188 9.439 6.683 0.006 -1.956 6.992 3.93 3.789 1.284 9.639 1.02(2) 9.940 4.66(4) 1.952 -0.182 8.285 1.833 4.188 1.791 10.807 3.32(4)	0 0.857 9 0.000 5 0.050 1 0.000 4 0.199 0 0.308 2 0.001 2 0.001 2 0.855 8 0.085 1 0.073 5 0.157 5 0.001	
	Boodhwani, 2000 Chistiansen, 2016 Colak, 2015 deTournay-Jette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Harmon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiene, 2019 Liu, 2009 Mu, 2013	0.500 1.900 7.300 -3.010 6.000 1.500 3.300 8.300 7.000 -0.200 4.000 2.000	10.530 110 1.091 1 1.539 2 1.528 2 1.168 1 3.234 10 2.425 5 1.500 2 1.500 2 1.500 4 1.117 4 1.117 1 1.413 1 2.045 4 1.290 1	.882 -18.739 191 5.161 308 -6.026 330 3.008 304 -0.789 400 -3.039 883 3.546 251 4.000 206 -2.352 736 -0.285 247 -0.188 998 -0.789	22.539 0.18(9.439 6.68) 9.439 6.68) 0.006 -1.95(6.69) 8.992 3.93; 3.789 1.28(9.63) 1.3054 3.422 9.940 4.60(1.952 -0.18) 1.952 -0.18; 4.769 1.416	0 0.857 9 0.000 1 0.000 1 0.000 4 0.199 0 0.308 0 0.001 5 0.000 2 0.855 0 0.000 1 0.073 5 0.157 5 0.001 0 0.003	
	Boodhwani, 2008 Chistiansen, 2016 Colsk, 2015 deTournay-Jette, 2011 Dong, 2014 Go to, 2000 Hall, 1999 Hammon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Norkiene, 2011 Reents, 2002 Restrepo, 2002	0.500 1.900 7.300 6.000 1.500 3.300 7.000 -0.200 4.000 2.000 2.000 6.800 2.400 0.570	10.530 110 1.091 1 1.539 2 1.528 2 1.168 1 3.234 1 0.2.425 5 1.500 2 1.170 4 1.117 1 1.413 1 2.045 4 1.290 1 2.465 4 1.290 1 2.465 4 1.246 4	.882 -18.739 191 5.181 368 -6.026 330 3.008 364 -0.789 .460 -3.039 .883 3.546 .251 4.000 .206 -2.352 .736 -0.265 .247 -0.188 .996 -0.789 .180 2.793 .080 -0.129 .075 -3.831 .315 -12.028	22.539 0.180 9.439 6.883 9.92 3.93 3.789 1.284 9.639 1.284 9.940 4.666 1.952 -0.183 8.285 1.831 4.188 1.799 4.769 1.180 1.0807 3.326 4.929 1.806 5.831 0.406 1.916 0.083	0 0.857 0 0.000 1 0.000 1 0.000 1 0.000 2 0.000 2 0.001 5 0.000 2 0.855 0 0.000 0 0.003 0 0	
	Boodhwani, 2000 Chistiansen, 2016 Colak, 2015 deTournay-Jette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Hammon, 2005 Kadoi, 2005 Kadoi, 201b Kumpaitiene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Nokiene, 2011 Reents, 2002 Restrepo, 2002 Soott, 2002	0.500 1.900 7.300 -3.010 6.000 1.500 8.300 7.000 -0.200 2.000 2.000 6.800 2.400 1.000 0.570 0.570 0.570	10.530 110 1.091 1 1.539 2 1.1529 2 1.168 1 3.234 10 2.425 5 1.500 2 1.098 1 2.176 4 1.117 1 1.413 1 2.045 4 1.290 1 2.495 6 6.428 41 0.392 0 1.313 1	.882 -18.739 191 5.101 308 -6.026 330 3.098 304 -0.789 .480 -3.039 304 -0.789 .480 -2.352 736 -0.285 247 -0.188 996 -0.789 180 2.793 .665 -0.129 075 -3.831 .315 -12.028 153 5.132 724 -2.593	22.539 0.188 9.439 6.689 0.006 -1.956 8.992 3.93' 3.789 1.28 9.639 1.20' 9.940 4.666 1.952 -0.182 8.265 1.833 4.188 1.79' 4.769 1.416 10.807 3.322' 4.929 1.80' 5.831 0.40' 13.168 0.688 15.055 2.553 0.018	0 0.857 9 0.000 1 0.000 1 0.000 1 0.000 1 0.000 2 0.308 2 0.001 5 0.000 2 0.855 3 0.085 1 0.073 3 0.157 5 0.001 0 0.003 3 0.885 9 0.988 1 0.003 1 0	
	Boodhwani, 2008 Chistiansen, 2016 Colak, 2015 deTournay-lette, 2011 Dong, 2014 Gob, 2000 Hall, 1999 Hamon, 2005 Kadoi, 2005 Kadoi, 2011b Kumpaitiene, 2019 Liu, 2009 Mu, 2013 Newman, 1987 Noriene, 2011 Reents, 2002 Restrepo, 2002 Scott, 2002	0.500 1.900 7.300 -3.010 6.000 1.500 8.300 7.000 -0.200 4.000 2.000 2.000 2.000 2.400 1.000 0.570 5.900	10.530 110 1.091 1 1.539 2 1.528 2 1.168 1 3.234 1 2.425 5 1.500 2 1.176 4 1.117 1 1.413 1 2.045 4 1.290 1 2.495 6 6.428 41 0.392 0 1.313 0	.882 -18.739 191 5.101 308 -6.026 330 3.008 304 -0.789 .480 -3.039 .883 3.546 .251 4.000 .206 -2.352 .247 -0.188 .996 -0.789 .085 -0.129 .075 -3.821 .085 -0.129 .075 -3.821 .085 -0.129 .075 -3.821 .085 -0.129 .085 -0.129	22.539 0.180 9.439 6.681 0.006 -1.956 8.992 3.93 3.789 1.28 9.639 1.20 13.054 3.422 9.940 4.666 1.962 -0.183 4.188 1.791 4.769 1.416 1.0807 3.421 4.929 1.850 5.831 0.400 13.168 0.668 15.056	0 0.857 0 0.000 1 0.000 1 0.000 1 0.000 2 0.001 5 0.000 2 0.855 0 0.000 1 0.073 0 0.001 0 0.003 0 0 0 0.003 0 0 0 0.003 0 0 0 0.003 0 0 0 0 0.003 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	

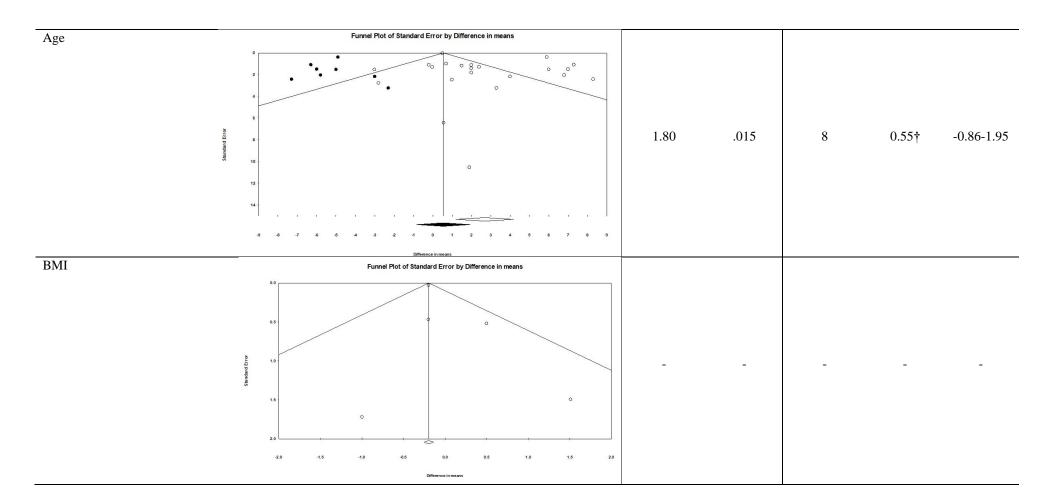
	Study name		_	Statistics for	oreach st	udy	-		-	Difference	e in means a	ind 95% CI	
		Difference in means	Standard	Variance	Lower	Upper limit	Z-Value	p-Value					
	Boodhwani, 2006	-0.200		0.001	-0.257	-0.143	-6.936	0.000	1	1		1	1
	deTournay-Jette, 2011	1.510		2.234	-1.420	4.440	1.010	0.312		_	00-01	\rightarrow	-
	Dong, 2014	0.500		0.271	-0.521	1.521	0.960	0.337			+	+	
	Mu, 2013	-0.200		0.220	-1.120	0.720	-0.426	0.670	,		•	-85	
	Norkiene, 2011	-1.000 -0.197		2.963 0.001	-4.374 -0.254	2.374 -0.141	-0.581 -6.874	0.561					7
		0.10	0.023	0.001		*****	0.014	0.000	-2.00	-1.00	0.00	1.00	2.00
									-2.00	-1.00	0.00	1.00	2.00
Cognition: All tests	Study name			Statistics fo	Accessed the latest					Std diff	in means a	nd 95% CI	
		Std diff in means	Standard error	Variance	Lower	Upper	Z-Value	p-Value					
	deTournay-Jette, 2011	0.823	0.344	0.119	0.148	1.498	2390	0.017	- 1	1	1-	_=	- 1
	Hall, 1999	0.237	0.346	0.120	-0.441	0.916	0.685	0.493					
	Kumpaitiene, 2019	-0.294	0.271	0.073	-0.824	0.236	-1.086	0.277		-	-		
		0.230	0.334	0.112	-0.425	0.884	0.687	0.492	1	J	-		
									-2.00	-1.00	0.00	1.00	2.00
Cognition: MMSE only	Study name			Statistics fo	(6)	10000				Differenc	e in means	and 95% CI	
		Difference in means	Standard error	Variance	Lower	Upper	Z-Value	p-Value					
	deTournay-Jette, 2011	1.110	0.453	0.205	0.223	1.997	2.452	0.014	1	1	1-		1
	Kumpaitiene, 2019	-0.600	0.550	0.302	-1.677	0.477	-1.092	0.275		¥ <u>-</u>		2 C	
	HAVENOR CALIFORNIAN	0.283	0.855	0.730	-1.391	1.958	0.332	0.740		10-	-		
									-4.00	-2.00	0.00	200	4.00
Depression: All tests	Study name		Statis	stics for ea	ach study	<u>.</u>				Std diff in	means and	d 95% CI	_
		diff Stan			wer Upp nit lin		Value p	Value					
										i	_	23	ñ
	Andrew Control						0.910 0.113	0.363		10.7			
	Haimon, 2005						7.807	0.000			-	_	
	Kadoi 2011h	2.024									0.000	0.00	
												344	
	Silbert, 2006	0.274	0.151	0.023 -0	023 0.	571	1.807	0.071				-	
	Silbert, 2006	0.274	0.151	0.023 -0	023 0.	571			4.00	200	000	2.00	400
	Silbert, 2006	0.274	0.151	0.023 -0	023 0.	571	1.807	0.071	-4.00	-2.00	0.00	2.00	4.00
Education (years)	Silbert, 2006	0.274	0.151 (0.499 (0.023 -0	023 0. 478 1.	571 479	1.807	0.071	-4.00		- 1700 P-20	2.00 s and 95% CI	100 400 5000
Education (years)	Silbert, 2006	0.274	0.151 0.499 d	0.023 -0. 0.249 -0. Statistics for	023 0. 478 1. oreach st	571 479 tudy Upper	1.807 1.003	0.071 0.316	-4.00		- 1700 P-20	17 45 601	100 400 5000
Education (years)	Silbert, 2006 Study name	0.274 0.501 Difference in means	0.151 0.499 d	0.023 -0. 0.249 -0. Statistics for	023 0. 478 1. oreach st	571 479 tudy	1.807 1.003	0.071 0.316	-4.00 I		- 1700 P-20	17 45 601	100 400 5000
Education (years)	Silbert, 2006	0.274 (0.501 (d. Difference	0.151 0.499 d	0.023 -0. 0.249 -0. Statistics for	023 0. 478 1. oreach st	571 479 tudy Upper limit	1.807 1.003 Z-Value -2.440	0.071 0.316 p-Value 0.015	4.00		- 1700 P-20	s and 95% CI	100 400 5000
Education (years)	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999	0.274 0.501 Difference in means -1.200 1.070 -1.600	0.151 0.499 0.499 0.492 0.492 0.913	0.023 -0. 0.249 -0. Statistics fi Variance 0.242 2.063 0.834	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390	571 479 Upper limit -0.236 3.885 0.190	7. Value 2. 440 0.745 -1.752	0.071 0.316 p-Value 0.015 0.456 0.080	4.00		- 1700 P-20	s and 95% CI	100 400 5000
Education (years)	Study name Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005	0.274 0.501	0.151 0.499 0.499 0.499 0.492 0.492 1.436 0.913 1.217	0.023 -0 0.249 -0 Statistics f Variance 0.242 2.063 0.834 1.480	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684	571 479 Upper limit -0.236 3.885 0.190 1.084	2.Value -2.440 0.745 -1.752 -1.069	0.071 0.316 p-Value 0.015 0.456 0.080 0.285	4.00		- 1700 P-20	s and 95% CI	100 400 5000
Education (years)	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019	Difference in means -1.200 -1.300 0.500	0.151 0.499 0 0.499 0 Standard error 0.492 1.436 0.913 1.217 1.327	0.023 -0 0.249 -0 Statistics f Variance 0.242 2.063 0.834 1.480 1.761	023 0. 478 1. bor each st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101	571 479 Upper limit -0.236 3.885 0.190 1.084 3.101	2.Value -2.440 0.745 -1.752 -1.069 0.377	p-Value 0.015 0.456 0.080 0.285 0.706	4.00		- 1700 P-20	s and 95% CI	100 400 5000
Education (years)	Study name Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005	0.274 0.501	0.151 0.499 0.499 0.499 0.492 0.492 1.436 0.913 1.217	0.023 -0 0.249 -0 Statistics f Variance 0.242 2.063 0.834 1.480	023 0. 478 1. 0r each st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446	571 479 Upper limit -0.236 3.885 0.190 1.084	2.Value -2.440 0.745 -1.752 -1.069	p-Value 0.015 0.456 0.080 0.285 0.706 0.261	4.00		- 1700 P-20	s and 95% CI	107691 2206
Education (years)	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019	Difference in means -1.200 -1.600 -1.300 0.600	0.499 6 Standard error 0.492 1.436 0.913 1.217 1.327 0.534	0.023 -0 0.249 -0 Statistics f. Variance 0.242 2.063 0.834 1.480 1.761 0.285	023 0. 478 1. 0r each st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446	571 479 Upper limit -0.236 3.885 0.190 1.084 3.101 1.646	2-Value 2.440 0.745 -1.752 -1.069 0.377 1.125	p-Value 0.015 0.456 0.085 0.706 0.285 0.706	4.00		- 1700 P-20	s and 95% CI	
Education (years)	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013	Difference in means -1.200 -1.600 -1.300 0.600	0.151 0.499 0.499 0.492 0.492 0.492 0.493 0.493	0.023 -0 0.249 -0 Statistics f: Variance 0.242 2.063 0.834 1.460 1.761 0.285 0.243	023 0. 478 1. Dereach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	571 479 Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	2-Value 2.440 0.745 -1.752 -1.069 0.377 1.125	p-Value 0.015 0.456 0.085 0.706 0.285 0.706	-	Differen	0.00	a and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpaitiene, 2019 Mu, 2013	0.274 0.501 Difference in means -1.200 -1.300 0.500 0.435	0.151 0.499 0.499 0.492 0.492 0.492 0.493 0.493	0.023 -0 0.249 -0 Statistics for Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243	023 0. 478 1. Dereach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	571 479 Upper limit -0.236 3.885 0.190 1.084 3.101 1.646 0.531	2-Value 2.440 0.745 -1.752 -1.069 0.377 1.125	p-Value 0.015 0.456 0.085 0.706 0.285 0.706	-	Differen	0.00	s and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diffe	0.274 0.501 Difference in means -1.200 -1.300 0.500 0.600 -0.435	0.151 0.499 0 Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	0.023 -0 0.249 -0 Statistics for Variance 0.242 2.063 0.834 1.460 1.761 0.285 0.243	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400	571 479 Upper limit -0.236 0.190 1.084 3.101 1.646 0.531	2-Value 2.440 0.745 -1.752 -1.069 0.377 1.125	p-Value 0.015 0.456 0.080 0.285 0.706 0.261 0.377	-	Differen	0.00	a and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diffe	0.274 0.501 Difference in means -1.200 -1.300 0.500 0.600 -0.435	0.151 0.499 0 Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493	0.023 -0 0.249 -0 Statistics for Variance 0.242 2.063 0.834 1.460 1.761 0.285 0.243	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stude	571 479 Upper limit -0.236 0.190 1.084 3.101 1.646 0.531	Z-Value 2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883	p-Value 0.015 0.456 0.080 0.285 0.706 0.261 0.377 p-Value 0.000	-	Differen	0.00	a and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diffs in 1 Colak, 2015 Dong, 2014	0.274 0.501 0.501 0.501 0.501 0.501 0.500 0.600 0.600 0.600 0.600	0.151 0.0499 0.051 0.0499 0.0510.051	0.023 -0 0.249 -0 0.249 -0 Variance 0.242 2.063 0.834 1.480 1.761 0.285 0.243 tistics for e	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 Deach stude Dower Ulimit 0.519 0.181	571 479 Upper limit -0.236 0.190 1.084 3.101 1.646 0.531 1.481 1.019	7. Value 2. 440 0. 745 -1. 752 -1. 069 0. 377 1. 125 -0. 883 2. Value 4. 075 2. 806	p-Value 0.015 0.285 0.706 0.261 0.377 p-Value 0.000 0.005	-	Differen	0.00	a and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diff. in: Colak, 2015 Dong, 2014 Mu, 2013	0.274 0.501 0.501 0.501 0.501 0.500 0.600 0.459	0.151 0.499 6 Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493 Standard error Value of the control o	0.023 -0 0.249 -0 0.249 -0 Statistics for 0.242 2.063 0.834 1.480 1.761 0.285 0.243 bistics for 0.243 Luriance 0.060 0.046 0.097	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 each stud ower U limit 0.519 0.181 -0.151	571 479 Upper limit -0.236 3.885 0.190 1.084 0.531 1.646 0.531 1.481 1.019 1.068	2.Value -2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 2.Value 4.075 2.806 1.475	p-Value 0.015 0.456 0.080 0.285 0.706 0.261 0.377 p-Value 0.000 0.005 0.140	-	Differen	0.00	a and 95% CI	4.00
	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diffs in 1 Colak, 2015 Dong, 2014	0.274 0.501 0.501 0.501 0.501 0.500 0.600 0.459 1.000	0.151 0.499 6 Standard error 0.492 1.436 0.913 1.277 1.327 0.534 0.493 Standard error Value 1.456 0.214 0.311 0.382	0.023 -0 0.249 -0 Statistics for expension of the control of the	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 Deach stude over limit 0.519 0.181 -0.151 0.252	571 479 Upper limit -0.236 3.885 0.190 1.084 0.531 V Upper limit 1.481 1.019 1.068 1.748	2.Value -2.440 0.745 -1.752 -1.083 2.Value 4.075 2.806 1.475 2.621	p-Value 0.015 0.456 0.080 0.261 0.377 p-Value 0.000 0.005 0.140 0.009	-	Differen	0.00	a and 95% CI	4.00
Education (years) EuroSCORE	Study name Colak, 2015 deTournay-Jette, 2011 Hall, 1999 Harmon, 2005 Kumpatiene, 2019 Mu, 2013 Study name Diff. in: Colak, 2015 Dong, 2014 Mu, 2013	0.274 0.501 0.501 0.501 0.501 0.500 0.600 0.459	0.151 0.499 6 Standard error 0.492 1.436 0.913 1.217 1.327 0.534 0.493 Standard error Value of the control o	0.023 -0 0.249 -0 0.249 -0 Statistics for 0.242 2.063 0.834 1.480 1.761 0.285 0.243 bistics for 0.243 Luriance 0.060 0.046 0.097	023 0. 478 1. Dreach st Lower limit -2.164 -1.745 -3.390 -3.684 -2.101 -0.446 -1.400 Deach stude over limit 0.519 0.181 -0.151 0.252	571 479 Upper limit -0.236 3.885 0.190 1.084 0.531 1.646 0.531 1.481 1.019 1.068	2.Value -2.440 0.745 -1.752 -1.069 0.377 1.125 -0.883 2.Value 4.075 2.806 1.475	p-Value 0.015 0.456 0.080 0.285 0.706 0.261 0.377 p-Value 0.000 0.005 0.140	-	Differen	0.00	a and 95% CI	4.00

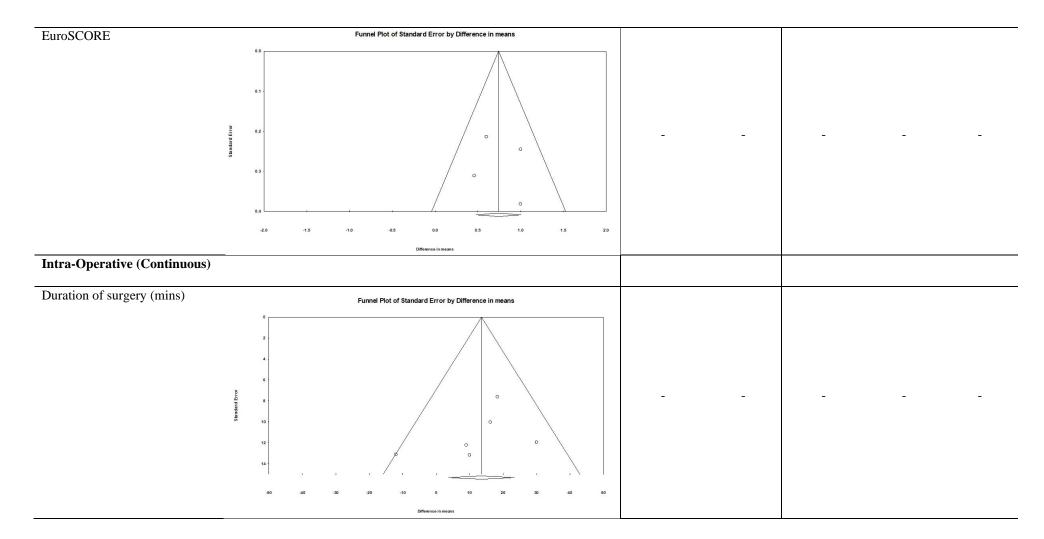


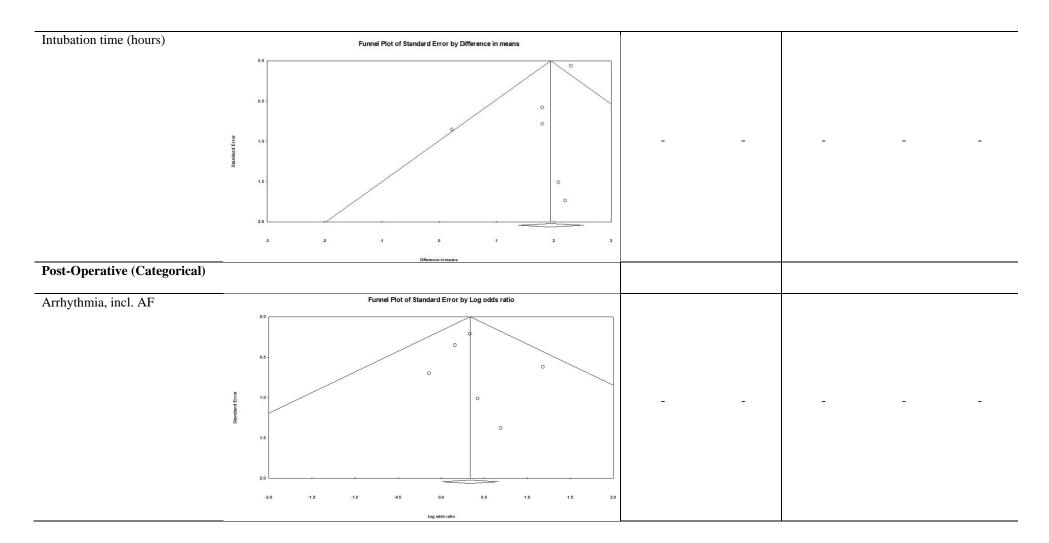
Number of grafts	Study name			Statist	cs for each	study				Differen	ce in means a	and 95% CI	
-		Difference in mean			Lower	Upper limit	Z-Value	p-Value					
	Boodhwani, 2006	0.0			000 -0.00		0.000	1.000	Ĩ	Î		ī	1
	Colak, 2015	0.1			008 -0.07		1.100	0.271			 -	-88	
	Dong, 2014	0.2			051 -0.24		0.884	0.377					15
	Harmon, 2005 Mu, 2013	0.2			188 -0.65 027 -0.12		0.461 1.212	0.645		88.			7
	Norkiene, 2011	0.3			038 -0.08		1.533	0.125			199		
	Reents, 2002	-0.2			083 -0.76		-0.693	0.489		_			
		0.0	25 0.	.030 0.	001 -0.03	0.085	0.842	0.400	1000		•		
									-1.00	-0.50	0.00	0.50	1.00
Total Microemboli	Study name			Statistic	s for each s	tudy				Std diff	in means an	id 95% CI	
		Std diff	Standard	l Variano	Lower e limit	Upper limit	Z-Value	n-Value					
	Liu, 2009	0.236	0.13			0.499	1.763	0.078	1	Ĭ			1
	Rodriguez, 2010	-0.055	0.10			0.154	-0.512	0.608				-	
	Royse, 2000	0.681	0.55			1.758	1.238	0.216					
	Stump, 1996	0.295	0.17	0 0.02	9 -0.038	0.627	1.736	0.082			-		
	100 market	0.157	0.11	3 0.01	3 -0.066	0.379	1.381	0.167			-	-	
									-1.00	-0.50	0.00	0.50	1.00
Post-Operative (Categorical)													
Arrhythmia, incl. AF	Study name			Statist	cs for e	ch stu	dy			Odds ra	atio and 9	95% CI	
				Lower	Upper								
			ratio	limit	limit	Z-Valu	ie p-V	alue	190	11 1000		9 900	
	Boodhwani, 20	006	1.398	0.922	2.122	1.5	76 0	.115	1	1 1	+	1	- 1
	Colak, 2015		1.176	0.591	2.342	0.46	62 0	.644		1 1		L	
	Mu, 2013		1.531	0.210	11.147	0.42	21 0	0.674					-
	Norkiene, 201	1	3.265	0.966	11.035	1.90		0.057		1 1			
	Restrepo, 2002		2.000	0.134	29.808	0.50		0.615	30				
	Suksompong,		0.870	0.220	3.435	-0.19		0.842					1
	SUNSUITIDUITY.	2002		1.013		2.03							
					1.941	2.0	36 (0.042	- 1	1 4.		1 1	8
			1.402	1.010					•				10
			1.402	1.010					0.1	0.2 0.5	5 1 2	2 5	
Delirium				NY 2520,425		-b -6:	.d		0.1 (10
Delirium	Study name	- 123233	s	tatistic	s for ea	ch stu	dy		0.1 (5 1 2		
Delirium		Od	S ds Lo	tatistic	s for ea Upper limit	ch stu Z-Valu	_	/alue	0.1 (
Delirium		Od ra	S ds Lo tio I	tatistic ower imit	Upper		ie b-/	/alue	0.1				
Delirium	Study name	Od ra 4.	S ds Lo tio I	ower imit 1.458	Upper limit	Z-Valu	ue p-\		0.1				
Delirium	Study name Colak, 2015 Norkiene, 20	Od ra 4.1	sds Lottio I	ower imit 1.458 1.076	Upper limit 11.935 75.621	Z-Val 0	ue p-\	0.008	0.1 (
Delirium	Study name	Od ra 4.: 11 9.0 2 39.0	Sds Lctio I	over imit 1.458 1.076 2.021 7	Upper limit 11.935 75.621 52.636	Z-Valu 2.66 2.02	ue p-\	0.008 0.043 0.015	0.1				
Delirium	Study name Colak, 2015 Norkiene, 20	Od ra 4.: 11 9.0 2 39.0	Sds Lctio I	over imit 1.458 1.076 2.021 7	Upper limit 11.935 75.621	Z-Val 0	ue p-\	0.008	0.1				**************************************
Delirium	Study name Colak, 2015 Norkiene, 20	Od ra 4.: 11 9.0 2 39.0	Sds Lctio I	over imit 1.458 1.076 2.021 7	Upper limit 11.935 75.621 52.636	Z-Valu 2.66 2.02	ue p-\	0.008 0.043 0.015	0.1	Odds ra	atio and		10
	Study name Colak, 2015 Norkiene, 20	Od ra 4.: 11 9.0 2 39.0	Sds Lctio I	over imit 1.458 1.076 2.021 7	Upper limit 11.935 75.621 52.636	Z-Valu 2.66 2.02	ue p-\	0.008 0.043 0.015		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 20 Reents, 2002	Od ra 4.: 11 9.0 2 39.0	Sds Lctio I	tatistic ower imit 1.458 1.076 2.021 7 2.322	Upper limit 11.935 75.621 52.636 16.269	Z-Valu 2.66 2.02 2.42 3.66	ue p-\	0.008 0.043 0.015		Odds ra	atio and	95% CI	
Post-Operative (Continuous) LOS in ICU (days)	Study name Colak, 2015 Norkiene, 20	Od ra 4.: 11 9.0 2 39.0 6.:	Sds Lottio I 171 019 000 2 147	ctatistic ower imit 1.458 1.076 2.021 7 2.322	Upper limit 11.935 75.621 52.636 16.269	Z-Valu 2.66 2.02 2.42 3.65	ue p-\	0.008 0.043 0.015		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Colak, 2015 Norkiene, 20 Reents, 2002	Od ra 4.: 11 9.0 2 39.0	Sds Lottio I 171 219 2000 21147 2	ctatistic ower imit 1.458 1.076 2.021 7 2.322	Upper limit 11.935 75.621 52.636 16.269	Z-Valu 2.66 2.02 2.42 3.65	ue p-\	0.008 0.043 0.015 0.000		Odds ra	atio and	95% CI	7
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006	Odd ra 4. 11 9.0 2 39.6.	Sds Lottio I 1771 :: 019 :: 0000 :: 1447 ::	1.458 1.076 2.021 7 2.322	Upper limit 11.935 75.621 52.636 16.269	Z-Valu 2.66 2.02 2.42 3.66 study Upper Upper limit 4 0.306	Je p-\ 62 (27 (26 (57 (Z-Value 36.220	0.008 0.043 0.015 0.000		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015	Od ra 4.11 9.02 39.06.	Sds Lotio I 1771 - 179 -	1.458 1.076 2.021 7 2.322 Statis dard for Vari	Upper limit 11.935 75.621 52.636 16.269 tics for each limit 0.000 0.22 0.021 0.002	Z-Valu 2.66 2.02 2.42 3.66 study Upper limit 4 0.306 5 0.588	Z-Value 36.220 2.060	0.008 0.043 0.015 0.000 0.000		Odds ra	atio and	95% CI	7
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006	Od ra 4: 11 9.0 2 39.0 6: Differe in mea	Section I 171 171 171 171 171 171 171 171 171 1	Statistic ower limit 1.458 1.076 2.021 7 2.322 Statis dard ror Vari 0.008 0.146 0.479	Upper limit 11.935 75.621 52.636 16.269	Z-Valu 2.66 2.02 2.42 3.65 study Upper limit 4 0.306 5 0.585 9 0.229	Z-Value 36.220 2.060	0.008 0.043 0.015 0.000		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 201 Harmon, 2005 Mu, 2013	Odd ra 4. 11 9.0 2 39.6. Differe in mee	Sds Lottio I 1771 179 0000 2 147 2 147 2 147 2 1000 1000 1000 1000 1000 1000 1000 10	Statistic Dwer Implementary Statistic Statis	Upper limit 11.935 75.621 52.636 16.269 tics for each Lowe limit 0.000 0.22 0.000 0.230 0.230 -1.6. 0.036 -0.25	Z-Valu 2.66 2.02 2.42 3.66 study Upper limit 4 0.306 5 0.585 9 0.229 4 0.444 2 0.228	Z-Value 36.220 2.060 -1.481 0.398 -1.010	p-Value 0.000 0.039 0.138 0.691 0.312		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 201 Harmon, 2005 Mu, 2013 Norkiene, 2011	Odd ra 4. 11 9.0 2 39.0 6.	Section IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	Statistic 1.458 1.076 2.021 7 2.322	Upper limit 11.935 75.621 52.636 16.269 Lics for each limit 0.000 0.27 0.021 0.00 0.230 -1.6 0.036 -0.24 0.036 -0.24 0.047 0.15	Z-Valu 2.66 2.02 2.42 3.66 study Upper limit 4 0.306 5 0.585 9 0.229 4 0.444 2 0.228 6 1.024	Z-Value 36.220 2.060 -1.481 0.398 -1.010 2.774	p-Value 0.000 0.039 0.691 0.312 0.006		Odds ra	atio and	95% CI	
Post-Operative (Continuous)	Study name Colak, 2015 Norkiene, 20 Reents, 2002 Study name Boodhwani, 2006 Colak, 2015 deTournay-Jette, 201 Harmon, 2005 Mu, 2013	Od ra 4. 11 9.0 2 39.0 6.	Section I 171 171 171 171 171 171 171 171 171 1	Statistic ower imit 1.458 1.076 2.021 7 2.322 Statis dard ord over 1.46 0.479 0.188 0.146 0.240 0.216 0.240	Upper limit 11.935 75.621 52.636 16.269 tics for each Lowe limit 0.000 0.22 0.000 0.230 0.230 -1.6. 0.036 -0.25	Z-Valu 2.66 2.02 2.42 3.66 study Upper limit 4 0.306 5 0.585 9 0.229 4 0.444 2 0.424 0 1.670	Z-Value 36.220 2.060 -1.481 0.398 -1.010 2.774 5.007	p-Value 0.000 0.039 0.138 0.691 0.312		Odds ra	atio and	95% CI	

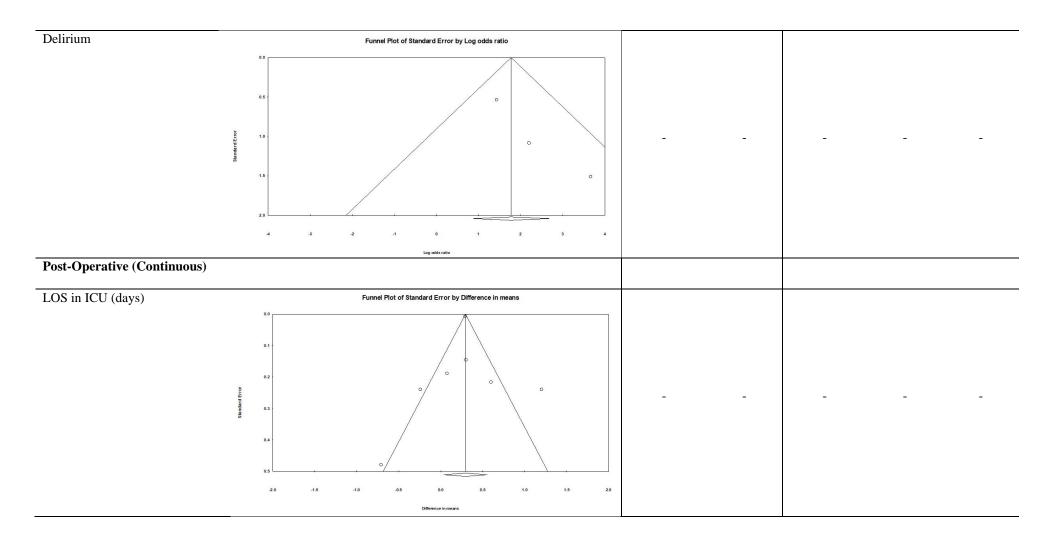
Figure S4. Funnel	plots for statistically significant analyses in regard to acute	Egger'	s Test	Т	rim and Fill	
•	oost-CABG, and results of publication bias/small-study effect more than 10 studies were available.	Intercept	p value (1-tailed)	No. imputed studies	OR/MD†	95%CI
Preoperative (Categor	rical)					
Depression	Only 2 studies, could not produce funnel plot			-	-	-
Diabetes	Funnel Plot of Standard Error by Log odds ratio	-0.39	.232	-	_	-











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

Variable	Forest Plot														
Pre-Operative (Categorical)															
Depression	Study name Compa	arison		Statist	ics fo	or each	study)dds ra	tio and	d 95% (<u> </u>	
				ower limit	Upp		.Value	p-Value							
	Kadoi, 2011b Blank		3.365	1.218		298	2.340	0.019	Ť	T	1	1.	1	- 1	_1
	5510-000#500-00000 FC-00000											:02	Τ.		-50
	Smith, 2000 Blank		2.000	0.825		851	1.533	0.125				1	7.		
			2.504	1.284	4.	883	2.693	0.007	I	-		-	-		13 (2)
									0.1	0.2	0.5	1	2	5	10
Diabetes	Study name	Compari	ison	S	Statist	ics for e	each stud	İγ		78	Odds ra	ntio and	1 95% C	Ĺ	
						Upper									
			rat	io li	mit	limit	Z-Valu	e p-Value							
	deTournay-Jette, 2011	Blank	0.7	19 0	0.237	2.179	-0.58	4 0.560		1,0	-+	-	-		
	Dieleman, 2009	Blank	1.4	103 0	0.384	5.131	0.51	2 0.609			-		+		
	Dijk, 2004	Blank	1.0	96 0	0.463	2.595	0.20	0.835			+	-	556		
	Kadoi, 2002	Blank	3.5	00 0	0.645	18.980	1.45	2 0.146				-	-	-	\rightarrow
	Kadoi, 2005	Blank	3.1	163 1	1.562	6.405	3.19	0.001	- 1			- 1	-	-	
	Kadoi, 2007	Blank	6.8	94 2	2.511	18.924	3.74	7 0.000					-	_	\mapsto
	Liu, 2009	Blank	0.3	375 0	0.104	1.347	-1.50	3 0.133	-	-	-				
	Mathew, 2006	Blank	1.0	50 0	0.366	3.014	0.09	0.927			-	-	1 40		
	Mathew, 2007	Blank	1.	38 0	0.762	1.701	0.63	2 0.527				-	-		
	Swaminathan, 2002	Blank	1.7	65 0	0.975	3.196	1.87	0.060				- F	-	8	
			1.5	36 0	0.984	2.396	1.89	0.059				4			
									0.1	0.2	0.5	1	2	5	10
Sex (male)	Study name	Comparis	son	St	tatisti	cs for ea	ach stud	у_			Odds ra	tio and	95% CI		
			Odd	s Lov	wer										
			rati	o lin	nit	limit	Z-Value	p-Value							
	deTournay-Jette, 2011	Blank	1.5	56 0	.359	6.739	0.59	0.555	- [-	+	+	+	1
	Dieleman, 2009	Blank	0.6	79 0	.256	1.802	-0.77	7 0.437		() -	- 1				
	Dijk, 2004	Blank	1.0	00 0	.531	1.884	-0.00	1.000			_	+	-		
	Kadoi, 2007	Blank	0.8	06 0	.324	2.007	-0.464	4 0.643			10 0	-	-		
	Kadoi, 2011b	Blank	1.0	46 0	.333	3.283	0.07	7 0.938			· -	_	-		
	Kadoi, 2005	Blank	0.6	76 0	.318	1.436	-1.01	0.309			-	+			
	Khatri, 1999	Blank	0.6	70 0	.331	1.354	-1.11	0.264			1	-			
	Mathew, 2007	Blank	1.2		.805	1.801	0.90	0.365							
	Mathew, 2006	Blank	1.0	00 0	.363	2.757	0.00	1.000				+	-		
	Smith, 2000	Blank	0.8	62 0.	.420	1.769	-0.40	0.686			200	•	-		
	Swaminathan, 2002	Blank	1.4	90 0	.868	2.558	1.44	7 0.148				+	+		
	Slater, 2009	Blank	0.8		.359	2.062	-0.33	0.735			+	-	-		
			1.0	05 0	.818	1.234	0.043	0.965					- 1		- 1

Study name		Statistic	s for ea	ach study	<u>/</u>	Odds ratio and 95% CI
1	Odds I	Lower I		Z-Value	p-Value	
deTournavalette 2011						1 1 1 4 6 1 1
Dieleman, 2009	0.901	0.342	2.375	-0.211	0.833	
Kadoi, 2001	0.200	0.100	0.400	-4.551	0.000	+
Kadoi, 2002	0.500	0.129	1.936	-1.003	0.316	
						<u>├ </u>
Mathew, 2007	1.000	0.689	1.450	-0.000	1.000	
Smith, 2000	1.000	0.581	1.722	0.000	1.000	-
Swaminathan, 2002						_ -\frac{1}{2}
	0.887	0.594	1.324	-0.586	0.558	
						0.1 0.2 0.5 1 2 5 10
Study name	Statis	stics fo	r each	study		Odds ratio and 95% CI
Odds ratio				Value p	-Value	
Mathew, 2006 0 643	0.24	6 1.6	76 -	0.904	0.366	- ■
0.003	0.56	00 1.3	13 -	0.555	0.560	
						0.1 0.2 0.5 1 2 5 10
Study name Compariso	<u>n</u>	Statist	ics for e	each study	_	Odds ratio and 95% CI
				7 Value	n Value	
					100	1 1 1 1
Matnew, 2007 Blank						
	0.027	0.200	2.020	-0.322	0.740	
						0.1 0.2 0.5 1 2 5 10
Study name Compariso	n	Statie	ice for	each etud	v	Odds ratio and 95% CI
Study Hame Compariso					L	odds fatto and 35% cf
			limit		p-Value	
Diik 2004 Blank						1 1 1 ± 1 1 1
ALL PROPERTY AND ADDRESS OF THE PROPERTY ADDRESS OF THE PROPERTY AND ADDRESS OF THE PROPERTY ADDRESS OF THE PR						💻 🗍
						0.1 0.2 0.5 1 2 5 10
						0.1 0.2 0.5 1 2 5 10
Study name	Statis	tics for	each	study		Odds ratio and 95% CI
Odds ratio	Lower			/alue p	-Value	
Djaiani, 2003 0.982	0.65			0.089	0.929	📠
				0.147	0.883	
	0 22			w. 171	0.000	
Kadoi, 2001 0.900	0.22			0 583	0.560	
Kadoi, 2001 0.900 Kadoi, 2002 0.700	0.21	1 2.32	22 -(0.583	0.560	
Kadoi, 2001 0.900 Kadoi, 2002 0.700 Kadoi, 2003 0.700	0.21	1 2.32 0 3.77	22 -(70 -(0.415	0.678	
Kadoi, 2001 0.900 Kadoi, 2002 0.700	0.21	1 2.32 0 3.73 5 2.44	22 -(70 -(45 (
	Kadoi, 2001	Study name Statistation Study name Comparison Odds ratio Dijk, 2004 Blank Dijk, 2004 Dijk	Dieleman, 2009	deTournay-Jette, 2011	Study name	Dieleman, 2009

Age (years)	Study name		_	itatistics for	each stu	xdy				Difference i	n means and	95% CI	
	23.	Difference in means	Standard	Variance	Lower	Upper	Z-Value p	Value					
	Braekken, 1998	7.605	8.935	48.090	-5.987	21.197	1.097	0.273	1 -		_		
	deTournay-Jette, 2011	-1.480	1.238	1.529	-3.903	0.943	-1.197	0.231		_	_		7
	Dieleman, 2009	0.200	2.171	4.713	4.055	4.455	0.092	0.927		- 10	-		
	Dijk, 2004	0.000	1,320	1.742	-2.587	2.587	0.000	1.000		_	+-	- 1	
	Kadoi, 2005	1.000	1.775	3.149	-2.478	4.478	0.564	0.573		_		→ _	
	Kadoi, 2007 Kadoi, 2011b	6.000 1.900	2.503 1.501	6.267 2.253	1,093	10.907	2,397 1,288	0.017					1
	Liu, 2009	4.300	1.935	3.746	0.507	8.093	2.222	0.026					
	Mathew, 2006	3.000	2.507	6.283	-1.913	7.913	1,197	0.231			_	•	-1
	Mathew, 2007	0.400	0.956	0.914	-1.474	2.274	0.418	0.676			_		
	Robson, 2000	4.000	2.847	8.103	-1.579	9.579	1.405	0.160	1			+	-1
	Swaminathan, 2002	1.093	0.589	1.615 0.346	-2.491	2.491	0.000	1,000	1	-		: I	
		1.000	0.000	0.010	-0.000	2.20	1.000	0.000	-8.00	4.00	0.00	4.00	8.00
									-8.00	4.00	0.00	4.00	8.00
Cognition: All tests	Study name			Statistics	for each	study				Std diff i	in means an	d 95% CI	
		Std diff	Standard		Lower	Upper							
	Wise Manual Manu	in means	emor	Variance	limit	limit	Z-Value	p-Value	200	200	200 0000	0.00	-
	deTournay-Jette, 2011	-0.256	0.267	0.071	-0.779	0.26	6 -0.96	1 0.336		-			
	Mathew, 2007	0.396	0.093	0.009	0.214	0.57	8 4.259	0.000			-		
	Swaminathan, 2002	0.483	0.123	0.015	0.241	0.72	4 3.912	0.000			15	-	
	CONTRACTOR OF THE CONTRACTOR O	0.303	0.148	0.022	0.013	0.59	3 2.048	0.041			-		
													Š.
									-1.00	-0.50	0.00	0.50	1.00
Cognition: CI only	Study name			Statistics fo	or each s	study				Differenc	e in means	and 95% CI	
,		Difference	Standard		Lower	Upper				200			
		in means	error	Variance	limit	limit	Z-Value	e p-Value					
	Mathew, 2007	0.189	0.044	0.002	0.103	0.27	5 4.29	7 0.000	- 1	1	1 4	- 1	- 4
	Swaminathan, 2002	0.880	0.222	0.049	0.445	1.31	5 3.96	6 0.000			18-	- 1	
		0.500	0.344	0.118	-0.174						100	_	
		0.500	0.544	0.110	-0.11	1.17	1.40	0.140		1			
									-1.00	-0.50	0.00	0.50	1.0
Depression: All tests	Study name		Si	atistics for	each st	tudy				Std diff i	n means ar	nd 95% CI	
Depression: All tests	s		andard	L	.ower	Upper	war the same			Std diff i	n means ar	nd 95% CI	
Depression: All tests	s		andard	L		AL DOLLAR STATE	Z-Value	p-Value	22	Std diff i	n means ar	nd 95% CI	
Depression: All tests	s		andard	L ariance	.ower	Upper	Z-Value 0.000	- CONTROL OF PARK	1	Std diffi	n means ar	nd 95% CI	Ĭ
Depression: All tests	S in Harmon, 2004	means 0.000	andard error \	L Variance 0.111	ower limit -0.653	Upper limit 0.653	0.000	1.000		Std diff i	in means ar	nd 95% CI	
Depression: All tests	Harmon, 2004 Kadoi, 2011b	0.000 2.532	andard error \ 0.333 0.313	/ariance 0.111 0.098	.ower limit -0.653 1.919	Upper limit 0.653 3.144	0.000 8.098	1.000 0.000		Std diff i	n means ar	nd 95% CI	- [
Depression: All tests	S in Harmon, 2004	0.000 2.532 0.060	0.333 0.313 0.172	0.111 0.098 0.029	.ower 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		Std diff i	n means ar	95% CI	-
Depression: All tests	Harmon, 2004 Kadoi, 2011b	0.000 2.532	andard error \ 0.333 0.313	0.111 0.098 0.029	.ower limit -0.653 1.919	Upper limit 0.653 3.144	0.000 8.098	1.000 0.000 0.728		Std diff i	n means ar	95% CI	-]
Depression: All tests	Harmon, 2004 Kadoi, 2011b	0.000 2.532 0.060	0.333 0.313 0.172	0.111 0.098 0.029	.ower 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		+	-	-
Depression: All tests	Harmon, 2004 Kadoi, 2011b	0.000 2.532 0.060	0.333 0.313 0.172	0.111 0.098 0.029	.ower 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	Std diff i	n means ar	2.00	4.0
	Harmon, 2004 Kadoi, 2011b	0.000 2.532 0.060	0.333 0.313 0.172	0.111 0.098 0.029	-0.653 1.919 -0.277 -0.675	Upper limit 0.653 3.144 0.396 2.386	0.000 8.098 0.348	1.000 0.000 0.728	-4.00	-2.00	+	2.00	4.0
	Harmon, 2004 Kadoi, 2011b Silbert, 2006	0.000 2.532 0.060 0.856	0.333 0.313 0.172 0.781	0.111 0.098 0.029 0.610	.ower limit -0.653 1.919 -0.277 -0.675	Upper limit 0.653 3.144 0.396 2.386 study r Upper	0.000 8.098 0.348 1.096	1.000 0.000 0.728 0.273	4.00	-2.00	0.00	2.00	4.0
	Harmon, 2004 Kadoi, 2011b Silbert, 2006	0.000 2.532 0.060 0.856	0.333 0.313 0.172 0.781	0.111 0.098 0.029 0.610 Statistics	ower limit -0.653 1.919 -0.277 -0.675	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit	0.000 8.098 0.348 1.096	1.000 0.000 0.728 0.273	4.00	-2.00	0.00	2.00	4.0
	Harmon, 2004 Kadoi, 2011b Silbert 2006 Study name Braekken, 1998	0.000 2.532 0.060 0.856 Difference in means	0.333 0.313 0.172 0.781	0.111 0.098 0.029 0.610 Statistics Variance 4 Variance	-0.653 1.919 -0.277 -0.675 for each Lowe limit 1 -11.9	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit limit 1.2	0.000 8.098 0.348 1.096	1.000 0.000 0.728 0.273	4.00	-2.00	0.00	2.00	4.0
	Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011	0.000 2.532 0.060 0.856 Difference in means	0.333 0.313 0.172 0.781 Standar error 00 3.38	0.111 0.098 0.029 0.610 Statistics 1 Variance 54 1125 4 124	-0.653 1.919 -0.277 -0.675 for each Lower limit 1 -11.91	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.234 2.8	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59	1.000 0.000 0.728 0.273	4.00	-2.00	0.00	2.00	4.0
Depression: All tests Education (years)	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006	0.000 2.532 0.060 0.856 Difference in means -5.34 0.65 -1.00	0.333 0.313 0.172 0.781 Standar error 0 3.34 0 1.1*	Color	ower limit -0.653 1.919 -0.277 -0.675 Lower limit 1 -11.9 1 -15.57 -225	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.234 2.8 95 0.2	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.50 34 0.58 95 -1.5'	1.000 0.000 0.728 0.273	4.00	-2.00	0.00	2.00	4.0
	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	Difference in means -0.000 -0.856 Difference in means -5.34 -0.656 -1.00 -0.40	0.333 0.313 0.172 0.781 Standarerror 0.333 0.172 0.781	Variance 0.111 0.098 0.029 0.610 Statistics 4 Variance 54 1125 14 124 31 0.433 22 0.888	-0.653 1.919 -0.277 -0.675 for each Lowe limit 1 -11.9 1 -1.53 7 -223 5 -0.17	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2:34 2.8:35 0.2:72 0.9	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.58 34 0.58 95 -1.57 72 1.37	1.000 0.000 0.728 0.273 e p-Value 92 0.111 33 0.560 13 0.130 71 0.170	-4.00	-2.00	0.00	2.00	4.0
	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006	Difference in means -5.34 -0.65 -1.00 -0.50	0.333 0.313 0.172 0.781 Standarerror 0.333 0.100 0.333 0.0000 0.00	Color Colo	-0.653 1.919 -0.277 -0.675 for each Lowe limit 1 -11.9 1 -1.5 7 -2.23 5 -0.17 2 -0.25	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2:34 2.8:35 0.2:72 0.9:39 1.2:	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 e p-Value 52 0.111 32 0.560 33 0.130 71 0.170 25 0.185	4.00	-2.00	0.00	2.00	4.0
	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	Difference in means -0.000 -0.856 Difference in means -5.34 -0.656 -1.00 -0.40	0.333 0.313 0.172 0.781 Standarerror 0.333 0.100 0.333 0.0000 0.00	Color Colo	-0.653 1.919 -0.277 -0.675 for each Lowe limit 1 -11.9 1 -1.5 7 -2.23 5 -0.17 2 -0.25	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2:34 2.8:35 0.2:72 0.9:39 1.2:	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 e p-Value 92 0.111 33 0.560 13 0.130 71 0.170 25 0.185	4.00	-2.00	0.00	2.00	4.0
	Sin Harmon, 2004 Kadoi, 2011b Silbert, 2006 Study name Braekken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007	Difference in means -5.34 -0.65 -1.00 -0.50	0.333 0.313 0.172 0.781 Standarerror 0.333 0.100 0.333 0.0000 0.00	Color	-0.653 1.919 -0.277 -0.675 for each Lowe limit 1 -11.9 1 -1.5 7 -2.23 5 -0.17 2 -0.25	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2:34 2.8:35 0.2:72 0.9:39 1.2:	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 e p-Value 52 0.111 32 0.560 33 0.130 71 0.170 25 0.185	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	Difference in means -5.34 -0.65 -1.00 -0.50	0.333 0.313 0.172 0.781 Standarerror 00 3.33 0 1.110 00 0.66 00 0.33 00 0.33	Color	1	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.2 2.8 4.1 2.8 2.8 2.0 2.0 2.0 2.0 3.7 3.7 0.8	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 e p-Value 52 0.111 32 0.560 33 0.130 71 0.170 25 0.185	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	4.00
Education (years)	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002	Difference in means -5.34 0.856 -1.00 0.40 0.550 0.13	0.333 0.313 0.172 0.781 Standard error 00 3.33 00 1.11 00 0.64 00 0.23 00 0.33	Color	1	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2 2.8 42 2.8 63 60 60 60 60 60 60 60 60 60 60 60 60 60	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 e p-Value 52 0.111 32 0.560 33 0.130 71 0.170 25 0.185	<u> </u>	-2.00 Difference	0.00	2.00 and 95% CI	
Education (years)	Study name Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002	Difference in means -5.34 0.856 -1.00 0.40 0.550 0.13	0.333 0.313 0.172 0.781 Standarderororo 0.338 0.172 0.781	Variance	0.000 0.00	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.2 4.4 2.8 4.5 2.0 9.9 9.1 2.0 9.9 9.1 2.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8	0.000 8.098 0.348 1.096 t t Z-Valu 34 -1.59 34 0.58 95 -1.5* 72 1.37 39 1.32	1.000 0.000 0.728 0.273 10 p-Value 10 p-Value 11 p-Value 12 p-Value 13 p-Value 14 p-Value 15 p-Value 16 p-Value 17 p-Value 18 p-Value 18 p-Value 19 p-Value 19 p-Value 19 p-Value 19 p-Value 10 p-Val	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002	Difference in means -0.000 -0.856 Difference in means -0.34 -0.656 -1.00 -0.40 -0.50 -0.13	0.333 0.313 0.172 0.781 Standarderororo 0.338 0.172 0.781	Continue	0.000 0.00	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.2 4.4 2.8 4.5 2.0 9.9 9.1 2.0 9.9 9.1 2.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8.0 8	0.000 8.098 0.348 1.096 1.096 2.159 34 -1.59 34 0.58 95 -1.57 72 1.33 39 1.32 27 0.36	1.000 0.000 0.728 0.273 10 p-Value 10 p-Value 11 p-Value 12 p-Value 13 p-Value 14 p-Value 15 p-Value 16 p-Value 17 p-Value 18 p-Value 18 p-Value 19 p-Value 19 p-Value 19 p-Value 19 p-Value 10 p-Val	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002	Difference in means -5.34 -0.60 0.40 0.50 0.13	andard error \ 0.333 \ 0.313 \ 0.172 \ 0.781 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	Statistics Sta	Ower Content Content	Upper limit 0.653 3.144 0.396 2.386	0.000 8.098 0.348 1.096 t Z-Valu 94 -1.5t 34 -1.5t 95 -1.5t 772 1.37 39 1.32 27 0.36	1.000 0.000 0.728 0.273 e p-Value 92 0.111 30 0.150 31 0.150 32 0.151 35 0.715	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Study name	Difference in means -5.34 -0.856 -1.000 0.13	andard error \ 0.333 \ 0.313 \ 0.172 \ 0.781 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	Company Comp	Ower Ilmit O.653 1.919 O.277 O.675 O.675	Upper limit 0.653 3.144 0.396 2.386	0.000 8.098 0.348 1.096 1.096 2.Value 95 -1.57 1.33 297 1.32 277 0.36	1.000 0.000 0.728 0.273 0.273 0.273 0.111 33 0.560 0.130 0.130 0.130 0.130 0.155 0.185 0.715	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Bracken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002 Study name Bracken, 1998 Study name	Difference in means -5.34 -0.65 -1.000 -0.13	0.333 0.313 0.172 0.781 Standard error 0.338 0.111 0.66 0.028 0.038 0.038	Color	1	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 1.2.2.8.8 0.22 0.22 0.23 0.25 0.25 0.25 0.25 0.25 0.25 0.25 0.25	0.000 8.098 0.348 1.096 1.096 1.59 34 -1.59 39 -1.57 72 1.37 39 1.37 39 1.37 39 1.37 39 1.37 39 1.37	1.000 0.000 0.728 0.273 de p-Value 22 0.111 33 0.550 71 0.130 72 0.135 35 0.715	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Mathew, 2007 Swaminathan, 2002 Study name Discussion of the state of th	Difference in means -5.34 0.856 Difference in means -5.34 0.85 -1.00 0.40 0.50 0.13	0.333 0.313 0.172 0.781 Standard error 0 3.33 0 1.11 0 0.61 0 0.21 0 0.33 0 0.33 0 0.33	Variance	1 - 11.9	Upper limit 0.653 3.144 0.396 2.386 study r Upper limit 14 1.2 2.8 44 2.8 45 0.2 2.9 99 1.2 0.9 1.2 1.114 5.765 3.875	0.000 8.098 0.348 1.096 1.096 1.096 1.096 1.096 1.37 2.7 2.7 2.7 2.7 2.7 2.7 2.7 2.7 2.7 2.	1.000 0.000 0.728 0.273 10 P-Value 92 0.111 33 0.560 13 0.130 17 0.170 25 0.185 35 0.715	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2006 Study name Study name Study name Study name Study name Display name Kadoi, 2005 Kadoi, 2007 Radoi, 2011b Mathew, 2006	Difference in means -2,000 1,000 -2,0	andard error \ 0.333 \ 0.313 \ 0.172 \ 0.781 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	Statistics Sta	1 -119	Upper limit 0.653 3.144 0.396 2.386	0.000 8.098 0.348 1.096 1.096 1.096 1.096 1.096 1.32 27 0.36 1.32 27 0.36	1.000 0.000 0.728 0.273 1.000 0.728 0.273 1.010 1.0170 1	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	
Education (years)	Study name Brackken, 1998 deTournay-Jette, 2011 Mathew, 2007 Swaminathan, 2002 Study name Di Kadoi, 2005 Kadoi, 2007 Kadoi, 2011b Mathew, 2008 Mathew, 2008 Mathew, 2008 Mathew, 2007	Difference in means -5.345 -0.050 0.856 Difference in means -5.345 -1.00 0.40 0.50 0.13	andard error \ 0.333 \ 0.313 \ 0.172 \ 0.781 \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	Statistics Sta	1 -119	Upper limit 0.653 3.144 0.396 2.386	0.000 8.098 0.348 1.096 1.096 2.Value 94 -1.55 34 -1.55 72 1.37 39 1.32 27 0.36	1.000 0.000 0.728 0.273 e p-Value 92 0.111 30 0.500 31 0.150 32 0.185 5 0.715	<u> </u>	-2.00 Difference	0.00 e in means a 0.00	2.00 and 95% CI	

ACC time (mins)	Study name			Statistics f	or each s	tudy				Difference	e in means a	nd 95% CI	
rice time (mms)	1	Difference	Standard		Lower	Upper	7111						
	12.1 70.1 22.22	in means	error	Variance		limit		p-Value	F2	61		10	. T
	Braekken, 1998	8.086				29.282	0.748	0.455		1 1000			
	Mathew, 2006	-4.300				5.724	-0.841	0.400	K	100			
	Mathew, 2007	-1.900				2.131	-0.924	0.356					
	Swaminathan, 2002	0.100				5.568 1.763	0.036	0.971		7552	- Tours		
		-1.29	1.538	2.429	-4.340	1./03	-0.829	0.407	L.				
									-10.00	-5.00	0.00	5.00	10.0
CPB time (mins)	Study name			Statistics	for each s	tudy				Difference	e in means a	nd 95% CI	
		Difference in means	Standard error	Variance	Lower	Upper	7.Value	p-Value					
	D								D.	1		L	J
	Braekken, 1998 Kadoi, 2005	5.159 8.000										9 5k	_ (
	Kadoi, 2005 Kadoi, 2007	3.00							- 1		903		- (
	Kadoi, 2011b	9.90							- 1		-	38	_1
	Mathew, 2006	-5.00							k-				225
	Mathew, 2007	-2.70		8.862					560		_	-	
	Swaminathan, 2002								k-	- =	9 Pa <u>ra</u>	1000	
		2.14	2.343	5.490	-2.444	6.741	0.917	0.359	- 1	I -			J
									-10.00	-5.00	0.00	5.00	10.0
Number of grafts	Study name			Statistics 1	for each s	tudy				Difference	e in means a	ind 95% CI	
	The bart destroy with a risk of the barts. The same	Difference in means	Standard error	Variance	Lower	Upper limit	Z-Value	p-Value					
	Dieleman, 2009	0.020	0.244	0.059	-0.458	0.497	0.081	0.935	1	I	-		1
	Mathew, 2006	-0.20	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	-0.10	0.110	0.012	-0.315	0.115	-0.913	0.361			-		
		-0.05	0.059	0.004	-0.171	0.062	-0.920	0.358			-		
									-1.00	-0.50	0.00	0.50	1.0
Total Microemboli	Study name			Statistics	for each :	study				Std diff	in means a	nd 95% CI	
	-	Std diff	Standard	1222	Lower	Upper		8200		93		390	
	1940 SISM 140NSSS	in means	error	Variance	limit	limit		p-Value	¥252	210			
	Braekken, 1998	-0.770	0.778	0.605		0.753			K	-	_1_		
	Liu, 2009	-0.076	0.244	0.059	-0.553	0.402	-0.310	0.756			_		
	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	K		_		
		-0.459	0.258	0.067	-0.965	0.048	-1.775	0.076				1	
									-2.00	-1.00	0.00	1.00	2
Post-Operative (Continuous)													
LOS in ICU (days)	Study name		<u>s</u>	tatistics for	r each st	ıdy				Difference	e in means	and 95% CI	
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \		ifference in means	Standard error	Variance	Lower	Upper limit	Z-Value	p-Value					
	Baba, 2007	0.880			0.338	1.422		THE PROPERTY OF	Ĩ	Ĭ	ř =		10
	CONTRACTOR SERVICE		0.276	0.076			3.185	0.001				8.	
	Dieleman, 2009	-0.470	0.371	0.137	-1.197	0.257	-1.268	0.205					
	1	0.228	0.675	0.455	-1.095	1.550	0.337	0.736	J.	V			- 6

Figure S6. Funnel p	olots for statistically significant analyses in regard to mid-term	Egger's Test	Trim and Fill	Trim and Fill			
_	est-CABG, and results of publication bias/small-study effect more than 10 studies were available.	p valu Intercept (1-taile	95%	бСI			
Preoperative (Categorie	cal)						
Depression	Only 2 studies, could not produce funnel plot						
Preoperative (Continuo	ous)						
Cognition: All tests	Funnel Plot of Standard Error by Std diff in means 0.0 0.1 0.2 0.3 0.4 2.0 1.5 1.0 0.5 1.0 1.5 2.0 Std diff in means						

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

Study name	Variable	Forest Plot
Odds Lower Upper ratio limit limit Z-Value P-Value	Pre-Operative (Categorical)	
Silbert, 2008	Cognitive Impairment	Study name Statistics for each study Odds ratio and 95% CI
Silbert, 2008 0.824 0.385 1.763 0.499 0.618 Trubnikova, 2014 1.339 0.563 3.189 0.660 0.509 0.1 0.2 0.5 1 2 5 10 10.18 0.574 1.803 0.060 0.952 0.1 0.2 0.5 1 2 5 10 10.18 0.574 1.803 0.060 0.952 0.1 0.2 0.5 1 2 5 10 10.18 0.574 1.803 0.060 0.952 0.1 0.2 0.5 1 2 5 10 0.1 0.2 0.5		
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		Silbert, 2008 0.824 0.385 1.763 -0.499 0.618
Study name		Trubnikova, 2014 1.339 0.563 3.189 0.660 0.509
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Dieleman, 2009 1,064 0,346 3,277 0,109 0,913	Diabetes	Study name Statistics for each study Odds ratio and 95% CI
Dieleman, 2009 1.064 0.346 3.277 0.109 0.913 1.435 0.781 2.636 1.164 0.245 0.1 0.2 0.5 1 2 5 10		
Lachmann, 2018 1.623 0.788 3.345 1.313 0.189		ratio limit Iimit Z-Value p-Value
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Study name Statistics for each study Odds ratio and 95% Cl		We provide the provide the provided to the pro
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Dieleman, 2009 0.819 0.365 1.837 -0.485 0.628	Sex (male)	Study name Statistics for each study Odds ratio and 95% CI
Dieleman, 2009 0.819 0.365 1.837 -0.485 0.628 Kok, 2017 5.230 0.271 101.100 1.095 0.274 1.170 0.279 4.906 0.215 0.830 O.1 0.2 0.5 1 2 5 10		
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Dieleman, 2009 1.612 0.758 3.427 1.241 0.215		0.1 0.2 0.5 1 2 5 10
Dieleman, 2009 1.612 0.758 3.427 1.241 0.215	Hypertension	Study name Statistics for each study Odds ratio and 95% CI
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 O.1 0.2 0.5 1 2 5 10 Pre-Operative (Continuous) Study name Difference in means and 95% CI 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		
Lachmann, 2018 1.163 0.685 1.975 0.560 0.576 1.296 0.840 1.998 1.171 0.241 O.1 0.2 0.5 1 2 5 10 Pre-Operative (Continuous) Study name Study name Standard In means Standard In means I		
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Pre-Operative (Continuous) Study name Statistics for each study Difference in means and 95% CI		01.02.05.1.2.5.10
Age (years) Study name Statistics for each study Difference in means and 95% CI		0.1 0.2 0.3 1 2 3 10
Difference in means Standard error Lower limit Upper 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	Pre-Operative (Continuous)	
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	Intra-Operative (Continuous)	

Number of grafts	Study name	Statistics for each study							Difference in means and 95% Cl					
		Difference in means	Standard error	Variance	Lower	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		2				
		0.032	0.152	0.023	-0.266	0.331	0.213	0.832	l,	g 8	-	-		
									-1.00	-0.50	0.00	0.50	1.00	