Supplemental Table 1: Neuropsychological testing in the 3 studies

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| **Study** | **Test battery** | **Control group** | **Definition of POCD** |
| **OCTOPUS** | Motor Choice Reaction TimeGrooved PegboardTrail Making Test Part A and BSymbol Digit ModalitiesStroop Color Word TestContinuous Performance TaskRey Auditory VerbaL LearningSelf-Ordering TasksVisual/Spatial Working MemorySternberg Memory Comparison TaskLine Orientation | No | Decrease of ≥20% on ≥3 neuropsychological tests at follow-up relative to baseline and/or stroke |
| **DECS** | Corsi Block TestRey Auditory Verbal LearningGrooved PegboardTrail Making Test A and BDigit Span | Yes | Z-score calculated for each test using Jacobson Truax RCI\* method.Z-score ≤ 1.96 on ≥2 tests and/or combined z-score ≤1.96 and/or stroke |
| **SuDoCo** | Visual Verbal Learning TestStroop Color WordMotor ScreeningPattern Recognition MemorySpatial Recognition MemoryChoice Reaction Time | Yes | Z-score calculated for each test using Rasmussen RCI\* method.Z-score ≤ 1.96 on ≥2 tests and/or combined z-score ≤1.96 |

\* The reliable change index is a value that differentiates real (clinically significant) change from fluctuations of an imprecise measurement instrument1 RCI calculation methods differ in their use of error estimates to eliminate methodological error in repeat neuropsychological testing2.

1 Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol. 1991 Feb;59(1):12–9.

2 Lewis MS, Maruff P, Silbert BS, Evered LA, Scott DA. The influence of different error estimates in the detection of postoperative cognitive dysfunction using reliable change indices with correction for practice effects. Arch Clin Neuropsychol. 2007 Feb;22(2):249–57.

Supplemental Table 2: Results of respective Model 3 (fully adjusted) in fixed-effects (as described in main text of manuscript) and random-effects inverse variance models.

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|  | **Model 3: Fixed-effects**  | **Model 3: Random-effects**  |
|  | Pooled OR (95% CI), p-value | Pooled OR (95% CI), p-value |
| **Diabetes and risk of POCD\*** | OR 1.84 (1.14, 2.97) p=0.01 | OR 1.84 (1.14, 2.97) p=0.01 |
| **Hypertension and risk of POCD\*** | OR 1.37 (0.91, 2.07) p=0.13 | OR 1.37 (0.91, 2.07) p=0.13 |
| **Obesity and risk of POCD\*** | OR 1.04(0.64, 1.69)p=0.88 | OR 1.04(0.64, 1.69)p=0.88 |
| **BMI and risk of POCD** | OR 1.02 (0.97, 1.07)p=0.47 | OR 1.02 (0.97, 1.07)p=0.47 |
| **Systolic blood pressure and risk of POCD** | OR 1.04 (0.93, 1.15) p=0.49 | OR 1.03 (0.89, 1.20)p=0.67 |
| **Diastolic blood pressure and risk of POCD** | OR 0.95 (0.79, 1.15) p=0.62 | OR 0.96 (0.75, 1.22)p=0.73 |

\*Model 3 based on a single model for these exposures

**Supplemental Table 3:** Association of BMI, systolic blood pressure and diastolic blood pressure with risk of POCD in each study, and pooled estimates

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| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OCTOPUS** |  | **DECS** |  | **SuDoCo** |  | **Pooled estimates** |
|  | **OR (95% CI)** | **p** | **Weight** |  | **OR (95% CI)** | **p** | **Weight** |  | **OR (95% CI)** | **p** | **Weight** |  | **OR (95% CI)** | **p** |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ***BMI and risk of POCD*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Model 0: no adjustment | 1.06 (0.98, 1.16) | 0.16 | 28.0% |  | 1.05 (0.93, 1.19) | 0.44 | 13.4% |  | 1.00 (0.94, 1.06) | 0.95 | 58.6% |  | *1.02 (0.98, 1.07)* | *0.33* |
|  Model 1: age, sex | 1.06 (0.98, 1.16) | 0.16 | 28.6% |  | 1.05 (0.93, 1.19) | 0.43 | 13.9% |  | 1.01 (0.95, 1.07) | 0.78 | 57.5% |  | *1.03(0.98, 1.08)* | *0.21* |
|  Model 2: +type of surgery, randomisation | 1.07 (0.98, 1.16) | 0.15 | 28.1% |  | 1.07(0.95, 1.20) | 0.29 | 14.2% |  | 1.01 (0.95, 1.07) | 0.71 | 57.7% |  | *1.03 (0.99, 1.08)* | *0.15* |
|  Model 3: +diabetes, hypertension | 1.05 (0.96, 1.14) | 0.32 | 29.5% |  | 1.04 (0.92, 1.19) | 0.54 | 13.6% |  | 1.00 (0.94, 1.06) | 0.96 | 56.9% |  | *1.02 (0.97, 1.07)* | *0.47* |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ***Systolic blood pressure and risk of POCD*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Model 0: no adjustment | 1.14 (1.01, 1.30) | 0.06 | 58.2% |  | -- |  |  |  | 0.96 (0.82, 1.12) | 0.60 | 41.8% |  | *1.06 (0.96, 1.17)* | *0.26* |
|  Model 1: age, sex | 1.12 (0.98, 1.29) | 0.10 | 56.7% |  | -- |  |  |  | 0.94 (0.80, 1.11) | 0.47 | 43.3% |  | *1.04 (0.94, 1.16)* | *0.46* |
|  Model 2: +type of surgery, randomisation | 1.12 (0.98, 1.29) | 0.10 | 57.2% |  | -- |  |  |  | 0.95 (0.81, 1.11)  | 0.52 | 42.8% |  | *1.04 (0.94, 1.16)* | *0.42* |
|  Model 3: +diabetes, obesity | 1.11 (0.97, 1.28) | 0.15 | 56.4% |  | -- |  |  |  | 0.95 (0.81, 1.12) | 0.55 | 43.6% |  | *1.04 (0.93, 1.15)* | *0.49* |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ***Diastolic blood pressure and risk of POCD*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  Model 0: no adjustment | 1.07 (0.82, 1.39) | 0.63 | 47.7% |  | -- |  |  |  | 0.81 (0.63, 1.04) | 0.10 | 52.3% |  | *0.92(0.77, 1.11)* | *0.38* |
|  Model 1: age, sex | 1.08 (0.83, 1.41) | 0.57 | 47.3% |  | -- |  |  |  | 0.83 (0.64, 1.07) | 0.15 | 52.7% |  | *0.94 (0.78, 1.13)* | *0.50* |
|  Model 2: +type of surgery, randomisation | 1.09 (0.83, 1.42) | 0.54 | 47.0% |  | -- |  |  |  | 0.84 (0.65, 1.08) | 0.17 | 53.0% |  | *0.95 (0.79, 1.14)* | *0.56* |
|  Model 3: +diabetes, obesity | 1.09 (0.83, 1.43) | 0.53 | 46.1% |  | -- |  |  |  | 0.85 (0.66, 1.10) | 0.21 | 53.9% |  | *0.95 (0.79, 1.15)* | *0.62* |

POCD determined at 12 months in OCTOPUS/DECS and at 3 months in SuDoCo. Blood pressure measured at baseline assessment before surgery. Data on blood pressure not available for DECS. Odds ratios correspond to 1 kg/m2 increment in BMI and 10 mmHg increment in blood pressure.