

Supplementary Materials

Near-Infrared Spectroscopy Monitoring in Cardiac and Noncardiac Surgery: Pairwise and Network Meta-Analyses

Christian Ortega-Loubon, Francisco Herrera-Gómez, Carolina Bernuy-Guevara, Pablo Jorge-Monjas, Carlos Ochoa-Sangrador, Juan Bustamante-Munguira, Eduardo Tamayo and F. Javier Álvarez.

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Material S1

Supplementary methods and search strategy

Full details on the methods followed are available to the reader from the online access link to the registered systematic review protocol in the International prospective register of systematic reviews PROSPERO:

Francisco Herrera-Gómez, Christian Ortega-Loubon, Coralina Bernuy-Guevara, Carlos Ochoa-Sangrador, Juan Bustamante-Munguira, Pablo Jorge-Monjas, Eduardo Tamayo, F. Javier Álvarez. Perioperative targets near-infrared spectroscopy values for cardiac and non-cardiac surgery patients: pairwise and network meta-analyses. PROSPERO 2019 CRD42019131417. Available from:

http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019131417

The published and unpublished literature sources interrogated, and the strategy designed and constructed at Pharmacological Big Data Laboratory, Pharmacology and Therapeutics, Faculty of Medicine, University of Valladolid, Spain, on the basis of search terms referred to the participants/population, intervention and study design are also available to the reader into the following panel (search results and formula):

PubMed
319221: "Thoracic Surgical Procedures"[MeSH Terms]
369697: "Cardiovascular Surgical Procedures"[MeSH Terms]
207356: "Cardiac Surgical Procedures"[MeSH Terms]
89485: "Myocardial Revascularization"[MeSH Terms]
428642: (("bypass"[Text Word]) OR "graft"[Text Word]) OR "grafting"[Text Word]
357261: (("valve"[Text Word]) OR "mitral"[Text Word]) OR "aortic"[Text Word]
66910: "Extracorporeal Circulation"[MeSH Terms] OR "Cardiopulmonary Bypass"[MeSH Terms]
45180: "extracorporeal"[Text Word]
2251: "intra aortic balloon pump"[Text Word]
84214: "Anastomosis, Surgical"[MeSH Terms]
75621: "anastomosis"[Text Word]
350277: "Digestive System Surgical Procedures"[MeSH Terms]
12718: "Elective Surgical Procedures"[MeSH Terms]
18432: "Laparotomy"[MeSH Terms]
21339: "Splenectomy"[MeSH Terms]
792: "Metastasectomy"[MeSH Terms]
712919: (((("gastric"[Text Word]) OR "biliary"[Text Word]) OR "pancreatic"[Text Word]) OR "colorectal"[Text Word]
29203: "splenectomy"[Text Word]
269744: "resection"[Text Word]
184638: "Neurosurgical Procedures"[MeSH Terms]
25363: "Pneumonectomy"[MeSH Terms]
82331: (((("lobectomy"[Text Word]) OR "craniotomy"[Text Word]) OR "craniectomy"[Text Word]) OR "decompression"[Text Word]
29560: ("pneumonectomy"[Text Word]) OR "segmentectomy"[Text Word]
289291: "Orthopedic Procedures"[MeSH Terms]

281836: ("knee"[Text Word]) OR "hip"[Text Word]
 32954: ("arthroscopy"[Text Word]) OR "arthroscopic"[Text Word]
 201582: "Organ Transplantation"[MeSH Terms]
 711049: (("transplantation"[Text Word]) OR "transplanted"[Text Word]) OR
 "transplant"[Text Word]
 12310: "Spectroscopy, Near-Infrared"[MeSH Terms]
 17817: ("near infrared spectroscopy"[Text Word]) OR "nirs"[Text Word]
 327739: "Clinical Trials as Topic"[MeSH Terms]
 132621: "Controlled Clinical Trials as Topic"[MeSH Terms]
 127557: "Randomized Controlled Trials as Topic"[MeSH Terms]
 99572: "Random Allocation"[MeSH Terms]
 1251537: (((("random"[Text Word]) OR "randomization"[Text Word]) OR
 "randomized"[Text Word]) OR "randomly"[Text Word])
 178207: ("Double-Blind Method"[MeSH Terms]) OR "Single-Blind Method"[MeSH
 Terms]
 322691: (("blind"[Text Word]) OR "blinded"[Text Word]) OR "masked"[Text Word]
 34399: "Placebos"[MeSH Terms]
 205494: "placebo"[Text Word]

Ovid

Journals@Ovid (Sumarios y Resúmenes todas las Revistas Ovid), Revistas Subscritas a Texto Completo por Sacyl, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to May 25, 2019

319194: exp Thoracic Surgical Procedures/
 369653: exp Cardiovascular Surgical Procedures/
 207341: exp Cardiac Surgical Procedures/
 89481: exp Myocardial Revascularization/
 963924: bypass.tw. or graft\$.tw.
 675360: valve.tw. or mitral.tw. or aortic.tw.
 66908: exp Extracorporeal Circulation/ or exp Cardiopulmonary Bypass/
 88362: extracorporeal.tw.
 9579: intra aortic balloon pump.tw.
 84196: exp Anastomosis, Surgical/
 142202: anastomosis.tw.
 350226: exp Digestive System Surgical Procedures/
 12714: exp Elective Surgical Procedures/
 18429: exp Laparotomy/
 21336: exp Splenectomy/
 792: exp Metastasectomy/
 1159695: gastric.tw. or biliary.tw. or pancreatic.tw. or colorectal.tw.
 43414: splenectomy.tw.
 608657: resection.tw.
 184569: exp Neurosurgical Procedures/
 25361: exp Pneumonectomy/
 180563: lobectomy.tw. or craniotomy.tw. or craniectomy.tw. or decompression.tw.
 23181: pneumonectomy.tw. or segmentectomy.tw.
 289209: exp Orthopedic Procedures/
 543893: knee.tw. or hip.tw.

62126: arthroscop\$.tw.
 201533: exp Organ Transplantation/
 1074634: transplant\$.tw.
 12306: exp Spectroscopy, Near-Infrared/
 23308: near infrared spectroscopy.tw. or nirs.tw.
 327595: exp Clinical Trials as Topic/
 132514: exp Controlled Clinical Trials as Topic/
 127452: exp Randomized Controlled Trials as Topic/
 99543: exp Random Allocation/
 2905965: random\$.tw.
 178161: exp Double-Blind Method/ or exp Dingle-Blind Method/
 1260536: blind\$.tw. or mask\$.tw.
 34396: exp Placebos/
 588826: placebo\$.tw.

Elsevier's Scopus

4662: KEY("thorax surgery") AND NOT INDEX (medline)
 2701: KEY("cardiovascular surgery") AND NOT INDEX(medline)
 14586: KEY("heart surgery") AND NOT INDEX(medline)
 5167: KEY("heart muscle revascularization") AND NOT INDEX(medline)
 236867: (TITLE-ABS-KEY(bypass) OR TITLE-ABS-KEY(graft*)) AND NOT INDEX(medline)
 198251: (TITLE-ABS-KEY(valve) OR TITLE-ABS-KEY(mitral) OR TITLE-ABS-KEY(aortic)) AND NOT INDEX(medline)
 10552: (KEY("extracorporeal circulation") OR KEY("cardiopulmonary bypass")) AND NOT INDEX(medline)
 14882: TITLE-ABS-KEY(extracorporeal) AND NOT INDEX(medline)
 650: TITLE-ABS-KEY("intra aortic balloon pump") AND NOT INDEX(medline).
 16785: KEY(anastomosis) AND NOT INDEX(medline)
 25639: TITLE-ABS-KEY(anastomosis) AND NOT INDEX(medline)
 5644: KEY("abdominal surgery") AND NOT INDEX(medline)
 6294: KEY("elective surgery") AND NOT INDEX(medline)
 15483: KEY(laparotomy) AND NOT INDEX(medline)
 5384: KEY(splenectomy) AND NOT INDEX(medline)
 564: KEY("metastasis resection") AND NOT INDEX(medline)
 195529: (TITLE-ABS-KEY(gastric) OR TITLE-ABS-KEY(biliary) OR TITLE-ABS-KEY(pancreatic) OR TITLE-ABS-KEY(colorectal)) AND NOT INDEX(medline)
 7523: TITLE-ABS-KEY(splenectomy) AND NOT INDEX(medline)
 101314: TITLE-ABS-KEY(resection) AND NOT INDEX(medline)
 15474: KEY(neurosurgery) AND NOT INDEX(medline)
 5077: KEY("lung resection") AND NOT INDEX(medline)
 43421: (TITLE-ABS-KEY(lobectomy) OR TITLE-ABS-KEY(craniotomy) OR TITLE-ABS-KEY(craniectomy) OR TITLE-ABS-KEY(decompression)) AND NOT INDEX(medline)
 3561: (TITLE-ABS-KEY(pneumonectomy) OR TITLE-ABS-KEY(segmentectomy)) AND NOT INDEX(medline)
 7945: KEY("orthopedic surgery") AND NOT INDEX(medline)
 127589: (TITLE-ABS-KEY(knee) OR TITLE-ABS-KEY(hip)) AND NOT INDEX(medline)
 14910: TITLE-ABS-KEY(arthroscop*) AND NOT INDEX(medline)

5900: KEY("organ transplantation") AND NOT INDEX(medline)
 168394: TITLE-ABS-KEY(transplant*) AND NOT INDEX(medline)
 13570: KEY("near infrared spectroscopy") AND NOT INDEX(medline)
 5567: TITLE-ABS-KEY(nirs) AND NOT INDEX(medline)
 26127: KEY("clinical trial (topic)") AND NOT INDEX(medline)
 1736: KEY("controlled clinical trial (topic)") AND NOT INDEX(medline)
 33114: KEY("randomized controlled trial (topic)") AND NOT INDEX(medline)
 13683: KEY(randomization) AND NOT INDEX(medline)
 1211201: TITLE-ABS-KEY(random*) AND NOT INDEX(medline)
 30368: (KEY("double blind procedure") OR KEY("single blind procedure")) AND NOT INDEX(medline)
 303111: (TITLE-ABS-KEY(blind*) OR TITLE-ABS-KEY(mask*)) AND NOT INDEX(medline)
 64114: KEY(placebo) AND NOT INDEX(medline)
 94263: TITLE-ABS-KEY(placebo) AND NOT INDEX(medline)

Web of Science

Web of Science Core Collection, Current Contents Connect, Derwent Innovations Index, KCI-Korean Journal Database, MEDLINE®, Russian Science Citation Index, SciELO Citation Index

864772: TOPIC: (bypass) OR TOPIC: (graft*)
 1205349: TOPIC: (valve) OR TOPIC: (mitral) OR TOPIC: (aortic)
 64984: TOPIC: (extracorporeal)
 3190: TOPIC: ("intra aortic balloon pump")
 112472: TOPIC: (anastomosis)
 1164321: TOPIC: (gastric) OR TOPIC: (biliary) OR TOPIC: (pancreatic) OR TOPIC: (colorectal)
 34282: TOPIC: (splenectomy)
 397960: TOPIC: (resection)
 133776: TOPIC: (lobectomy) OR TOPIC: (craniotomy) OR TOPIC: (craniectomy) OR TOPIC: (decompression)
 32914: TOPIC: (pneumonectomy) OR TOPIC: (segmentectomy)
 459043: TOPIC: (knee) OR TOPIC: (hip)
 45282: TOPIC: (arthroscop*)
 1208997: TOPIC: (transplant*)
 35045: TOPIC: ("near infrared spectroscopy") OR TOPIC: (nirs)
 2457139: TOPIC: (random*)
 1016208: TOPIC: (blind*) OR TOPIC: (mask*)
 315421: TOPIC: (placebo*)

Cochrane Controlled Register of Trials (CENTRAL)

14931: MeSH descriptor: [Thoracic Surgical Procedures] explode all trees
 18619: MeSH descriptor: [Cardiovascular Surgical Procedures] explode all trees
 12443: MeSH descriptor: [Cardiac Surgical Procedures] explode all trees
 8987: MeSH descriptor: [Myocardial Revascularization] explode all trees
 36950: (bypass):ti,ab,kw OR (graft):ti,ab,kw OR (grafting):ti,ab,kw
 14535: (valve):ti,ab,kw OR (mitral):ti,ab,kw OR (aortic):ti,ab,kw

 MeSH descriptor: [Extracorporeal Circulation] explode all trees (a)

MeSH descriptor: [Cardiopulmonary Bypass] explode all trees (b)
3890: a OR b

3987: (extracorporeal):ti,ab,kw
279: ("intra-aortic balloon pump"):ti,ab,kw
2102: MeSH descriptor: [Anastomosis, Surgical] explode all trees
3967: (anastomosis):ti,ab,kw
13022: MeSH descriptor: [Digestive System Surgical Procedures] explode all trees
1845: MeSH descriptor: [Elective Surgical Procedures] explode all trees
708: MeSH descriptor: [Laparotomy] explode all trees
175: MeSH descriptor: [Splenectomy] explode all trees
11: MeSH descriptor: [Metastectomy] explode all trees
52804: (gastric):ti,ab,kw OR (biliary):ti,ab,kw OR (pancreatic):ti,ab,kw OR
(colorectal):ti,ab,kw
658: (splenectomy):ti,ab,kw
20371: (resection):ti,ab,kw
5605: MeSH descriptor: [Neurosurgical Procedures] explode all trees
506: MeSH descriptor: [Pneumonectomy] explode all trees
5226: (lobectomy):ti,ab,kw OR (craniotomy):ti,ab,kw OR (craniectomy):ti,ab,kw OR
(decompression):ti,ab,kw
872: (pneumonectomy):ti,ab,kw OR (segmentectomy):ti,ab,kw
11550: MeSH descriptor: [Orthopedic Procedures] explode all trees
41269: (knee):ti,ab,kw OR (hip):ti,ab,kw
3974: (arthroscopy):ti,ab,kw OR (arthroscopic):ti,ab,kw
5434: MeSH descriptor: [Organ Transplantation] explode all trees
35657: (transplantation):ti,ab,kw OR (transplanted):ti,ab,kw OR (transplant):ti,ab,kw
299: MeSH descriptor: [Spectroscopy, Near-Infrared] explode all trees
1282: ("near-infrared spectroscopy"):ti,ab,kw OR (nirs):ti,ab,kw
40986: MeSH descriptor: [Clinical Trials as Topic] explode all trees
7764: MeSH descriptor: [Controlled Clinical Trials as Topic] explode all trees
7674: MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees
20584: MeSH descriptor: [Random Allocation] explode all trees
899229: (random):ti,ab,kw OR (randomization):ti,ab,kw OR (randomized):ti,ab,kw OR
(randomly):ti,ab,kw

MeSH descriptor: [Double-Blind Method] explode all trees (c)

MeSH descriptor: [Single-Blind Method] explode all trees (d)

150464: c or d

345626: (blind):ti,ab,kw OR (blinded):ti,ab,kw OR (masked):ti,ab,kw

23507: MeSH descriptor: [Placebos] explode all trees

270449: (placebo):ti,ab,kw

Study registries

ClinicalTrials.gov, the EU Clinical Trials Register, the United Kingdoms' ISRCTN
registry

1087: bypass

3044: graft

Also searched for Grafting in ClinicalTrials.gov

1876: valve

364: mitral

1825: aortic

Also searched for Aorta in ClinicalTrials.gov

522: extracorporeal

15: "intra aortic balloon pump"

Also searched for Balloon pump in ClinicalTrials.gov

380: anastomosis

Also searched for Anastomotic in ClinicalTrials.gov

4431: gastric

Also searched for Stomach and Gastro in ClinicalTrials.gov

1351: biliary

4720: pancreatic

Also searched for Pancreas in ClinicalTrials.gov

5555: colorectal

44: splenectomy

3183: resection

Also searched for Removal, Excisions, and Resected in ClinicalTrials.gov

124: lobectomy

126: craniotomy

24: craniectomy

220: decompression

24: pneumonectomy

27: segmentectomy

4133: knee

2154: hip

233: arthroscopy

304: arthroscopic

270: "near infrared spectroscopy"

222: nirs

60663: random or randomization

Also searched for Randomized in ClinicalTrials.gov

16: randomly

27858: blind

3899: blinded

1444: masked

Also searched for Mask in ClinicalTrials.gov

24503: placebo

Also searched for Placebo-controlled in ClinicalTrials.gov

DART Europe E-Theses Portal

1164: bypass
1515: graft
943: valve
221: mitral
1113: aortic
181: extracorporeal
8: "intra aortic balloon pump"
220: anastomosis
1073: gastric
328: biliary
1287: pancreatic
1630: colorectal
47: splenectomy
876: resection
23: lobectomy
20: craniotomy
7: craniectomy
202: decompression
15: pneumonectomy
2: segmentectomy
1103: knee
0: hip
66: arthroscopy
61: arthroscopic
229: "near infrared spectroscopy"
188: nirs
9304: random or randomization or randomized
2278: randomly
1409: blind
282: blinded
321: masked
1320: placebo

Open Access Theses and Dissertations (OATD)

5277: bypass
5617: graft
5673: valve
920: mitral
4189: aortic
562: extracorporeal
24: "intra aortic balloon pump"
723: anastomosis
4896: gastric
1013: biliary
5338: pancreatic
5732: colorectal

156: splenectomy
2815: resection
116: lobectomy
120: craniotomy
36: craniectomy
891: decompression
43: pneumonectomy
9: segmentectomy
7134: knee
7969: hip
226: arthroscopy
258: arthroscopic
1178: "near infrared spectroscopy"
777: nirs
72978: random or randomization or randomized
29399: randomly
9274: blind
1761: blinded
2293: masked
6568: placebo

Meeting abstracts archives

The World Heart and Cardiothoracic Surgery Conference to 2018, World Congress of Surgery to 2018, and World Congress of Anaesthesiologists to 2018.

233: manual searches.

Table S1. Participants, interventions, comparators, and outcomes in the included trials.

Trial Details	Design	Follow-up (days)	Participants/Population Characteristics	Interventions (n)	Comparators (n)	Outcomes	Cointerventions
Colak et al., 2015 [1] NCT00917124 Croatia	RCT	7	≥65 years/male/DM (%): 41.0/78.0/34.2 Operation: CABG with CPB. NIRS: INVOS system.	bSO ₂ >80% ^s (94)	No NIRS monitoring (96)	Neurocognitive impairment (MMSE, CTT1, GP), MACE, BPN, HD, PMV, ICU/hospital LOS.	None
NORMOSAT [2] NCT01432184 Canada	RCT	30	≥65 years/male/DM (%): 66.0/72.1/29.4 Operation: CABG + VR/r, multiple VR/r, Redo. NIRS: INVOS and non-INVOS systems.	Non-drop bSO ₂ >20% ^s (102)	No NIRS monitoring objectives (99)	Delirium ^e , death, MACE, arrhythmia, BPN, AKI, PMV, ICU/hospital LOS, readmission.	None
Kara et al., 2016 [3] Turkey	RCT	7-10	≥65 years/male/DM (%): 36.5/78.5/30.4 Operation: CABG with CPB. NIRS: INVOS system.	Non-drop bSO ₂ >20% ^s (43)	No NIRS monitoring (36)	Neurocognitive impairment (MoCa), ICU/hospital LOS.	None
Mohandas et al., 2013 [4] India	RCT	90	≥65 years/male/DM (%): 13.5/58.0/0.0 Operation: CABG with CPB. NIRS: non-INVOS system.	bSO ₂ >85% ^s (50)	No NIRS monitoring objectives (50)	Neurocognitive impairment (MMSE, ASEM).	None
Slater et al., 2009 [5] USA	RCT	90	≥65 years/male/DM (%): 38.0/84.0/35.0 Operation: CABG with CPB. NIRS: INVOS system.	Non-drop bSO ₂ >20% ^s (125)	No NIRS monitoring objectives (115)	Neurocognitive impairment ^e , delirium (DRS), hospital LOS.	None
Murkin et al., 2007 [6] Canada	RCT	30	≥65 years/male/DM (%): 24.0/88.0/21.0 Operation: CABG with CPB. NIRS: INVOS system.	bSO ₂ >75% ^s (100)	No NIRS monitoring objectives (100)	Death, MACE, arrhythmia, HD, PMV, ICU/hospital LOS, readmission.	None
Vretzakis et al., 2013 [7] NCT00879463 Greece	RCT	30	≥65 years/male/DM (%): 27.7/83.0/23.4 Operation: CABG with CPB. NIRS: INVOS system.	Non-drop bSO ₂ >20% ^s (75)	No NIRS monitoring objectives (75)	Neurocognitive impairment ^e , death, MACE, HD, PMV, ICU/hospital LOS.	NIRS-guided transfusions.

PASPORT [8] ISRCTN 23557269 UK	RCT	90	≥65 years/male/DM (%): 19.0/68.0/8.8 Operation: CABG with CPB. NIRS: INVOS system.	bSO ₂ >70% [§] (98)	No NIRS monitoring (106)	Neurocognitive impairment [¶] , death, MACE, BPN, AKI, biomarkers [£] .	hematocrit- guided transfusions.
Cowie et al., 2014 [9] Australia	RCT	30	≥65 years/male/DM (%): 40.0/50.0/10.0 Operation: colorectal, orthopedic. NIRS: INVOS system.	bSO ₂ >75% [§] (20)	No NIRS monitoring (20)	Death, MACE, AKI, hospital LOS, readmission.	None
Ballard et al., 2012 [10] ISRCTN39503939 UK	RCT	364	≥65 years/male/DM (%): 100.0/38.5/10.0 Operation: abdominal, orthopedic. NIRS: non-INVOS system.	Non-drop bSO ₂ >15% [§] (22)	No NIRS monitoring (29)	Neurocognitive impairment (MMSE), biomarkers [£] .	None
Casati et al., 2007 [11] USA	RCT	7-20	≥65 years/male/DM (%): 100.0/38.5/0.0 Operation: abdominal. NIRS: INVOS system.	bSO ₂ >75% [§] (56)	No NIRS monitoring objectives (66)	Neurocognitive impairment (MMSE), ICU/hospital LOS.	None
Cox et al., 2018 [12] Netherlands	RCT	42	≥65 years/male/DM (%): 40.0/65.5/0.0 Operation: Orthopedic. NIRS: non-INVOS system.	Non-drop bSO ₂ >20% [§] (20)	No NIRS monitoring objectives (20)	Neurocognitive impairment (MoCa).	None

[§]Target values were set on the basis of baseline bSO₂ measurement. [¶]standard scale use was not informed or not used. [£]serum S100B and IL-6 and urinary NGAL protein were dosed for detecting, respectively, brain injury, systemic inflammation and AKI in PASPORT study; only serum S100B was dosed in the study of Ballard et al., 2012 (reference 10). Abbreviations: AKI, acute kidney injury; ASEM, antisaccadic eye movement test; BPN, blood product need; bSO₂, brain oxygen saturation; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; DM, diabetes mellitus; DRS, Delirium Rating Scale; GP, Grooved-Pegboard test; GTT1, Color Trail Test 1; HD, hemodialysis; ICU, intensive care unit; INVOS, IN Vivo Optical Spectroscopy; LOS, length of stay; MACE, major adverse cardiovascular event; MMSE, Mini-Mental State Examination; MoCa, Montreal Cognitive Assessment test; NIRS, near-infrared spectroscopy; NORMOSAT, NORMal cerebral Oxygen SATuration; PASPORT, PATient-Specific cerebral oxygentation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; PMV, prolonged mechanical ventilation; RCT, randomized controlled trial; redo; re-operative cardiac surgery; VR/r, valve replacement or repair.

Table S2. Participants, interventions, comparators, and outcomes in trials eligible but not providing numerical data for the analysis.

Trial Details	Design	Follow-up (days)	Participants/Population Characteristics	Interventions (n)	Comparators (n)	Outcomes	Cointerventions
Deschamps et al., 2013 [13] Canada	RCT	7	≥65 years/male/DM (%): 66.0/72.1/29.4 Operation: CABG + VR/r, multiple VR/r, Redo. NIRS: INVOS and non-INVOS systems.	Non-drop bSO ₂ >20% [§] (23)	No NIRS monitoring objectives (25)	BPN, PMV, ICU/hospital LOS, readmission.	None
Harilall et al., 2014 [14] South Africa	RCT	30	≥65 years/male/DM (%): 51.0/70.0/19.0 Operation: CABG with CPB. NIRS: INVOS system.	bSO ₂ >75% [§] (20)	No NIRS monitoring (20)	MAP, temperature, pCO ₂ , hematocrit, biomarkers [¥] .	None
Trafidlo et al., 2015 [15] Poland	RCT	42	≥65 years/male/DM (%): 20.0/70.0/10.0 Operation: lumbar spine surgery. NIRS: INVOS system.	bSO ₂ >75% [§] (13)	No NIRS monitoring (30)	Neurocognitive impairment (MMSE).	None

[§]Target values were set on the basis of baseline bSO₂ measurement. [¥]only serum S100B was dosed.

Table S3. Risk of bias in studies eligible.

Trials	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Colak et al., 2015 [1]	L	L	L	U	U	L	U
NORMOSAT [2]	L	L	L	L	U	L	U
Kara et al., 2016 [3]	L	L	L	L	L	L	U
Mohandas et al., 2013 [4]	L	L	U	U	U	L	U
Slater et al., 2009 [5]	L	L	L	L	L	L	U
Murkin et al., 2007 [6]	L	L	U	U	U	L	U
Vretzakis et al., 2013 [7]	L	L	U	U	U	L	U
PASPORT [8]	L	L	L	U	U	L	U
Cowie et al., 2014 [9]	L	L	L	L	U	L	U
Ballard et al., 2012 [10]	L	L	U	U	U	U	U
Casati et al., 2007 [11]	L	L	U	U	U	U	U
Cox et al., 2018 [12]	L	L	U	U	L	U	U
Deschamps et al., 2013 [13]	L	L	U	U	U	L	U
Harilall et al., 2014 [14]	L	L	U	U	L	U	U
Trafidlo et al., 2015 [15]	L	L	U	U	U	U	U

The judgement for each of risk of bias domain is presented as (L), (U) or (H) to indicate low, unclear, or high risk of bias, respectively.

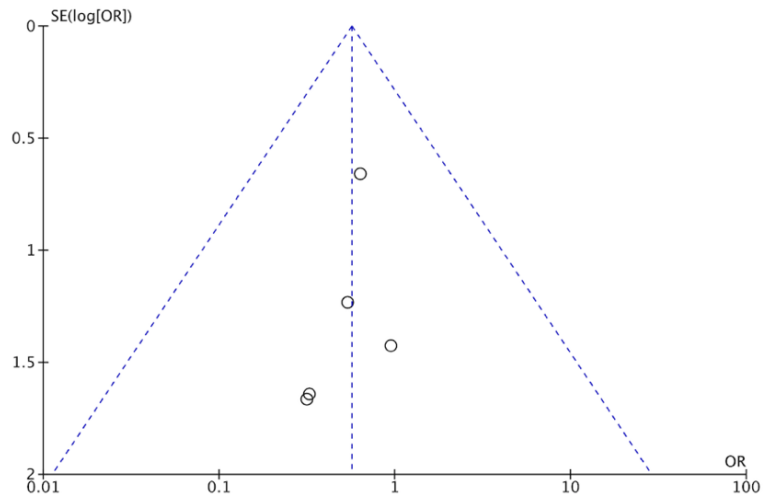
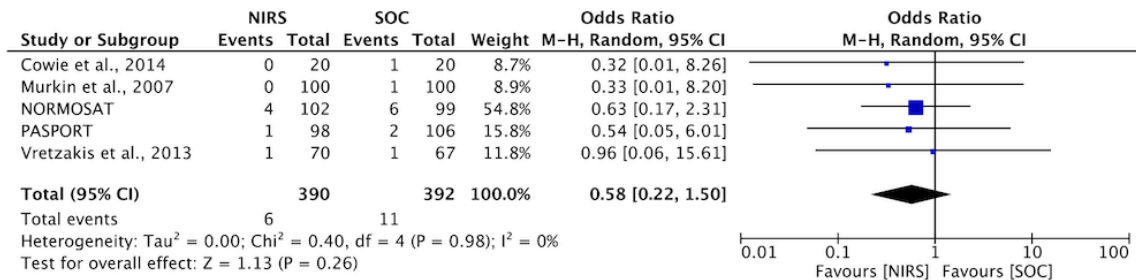


Figure S1. The effect of NIRS monitoring on post-operative death. CI, confidence interval; M-H, Mantel-Haenszel test; NIRS, near-infrared spectroscopy; NORMOSAT, NORMAL cerebral Oxygen SATuration; PASPORT, PATient-Specific cerebral oxygenation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; SE, standard error; SOC, standard of care.

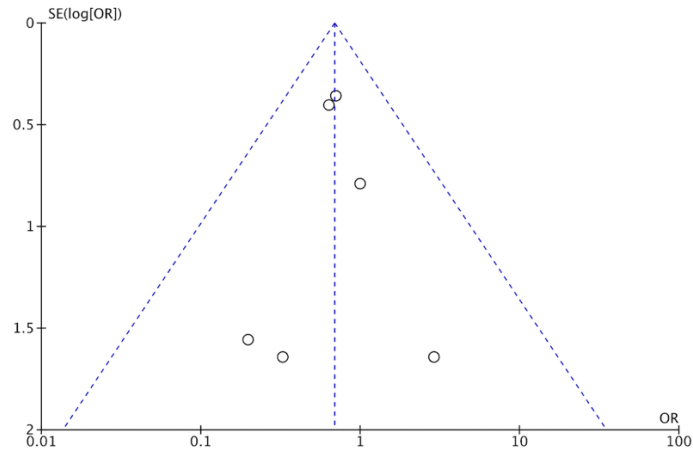
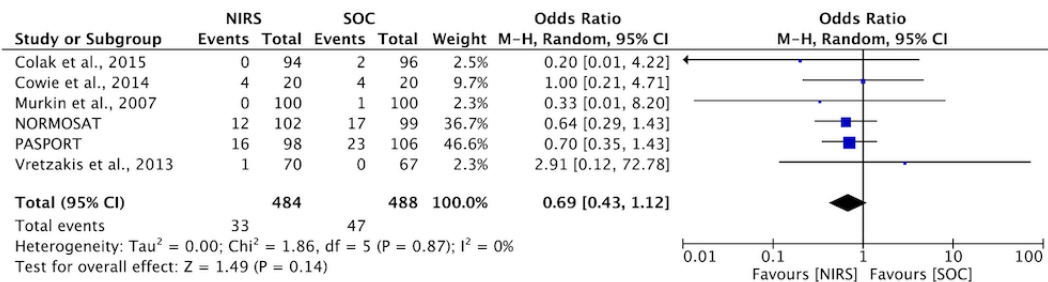


Figure S2. The effect of NIRS monitoring on post-operative AKI. AKI, acute kidney injury; CI, confidence interval; M-H, Mantel-Haenszel test; NIRS, near-infrared spectroscopy; NORMOSAT, NORMAl cerebral Oxygen SATuration; PASPORT, PATient-Specific cerebral oxygenation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; SE, standard error; SOC, standard of care.

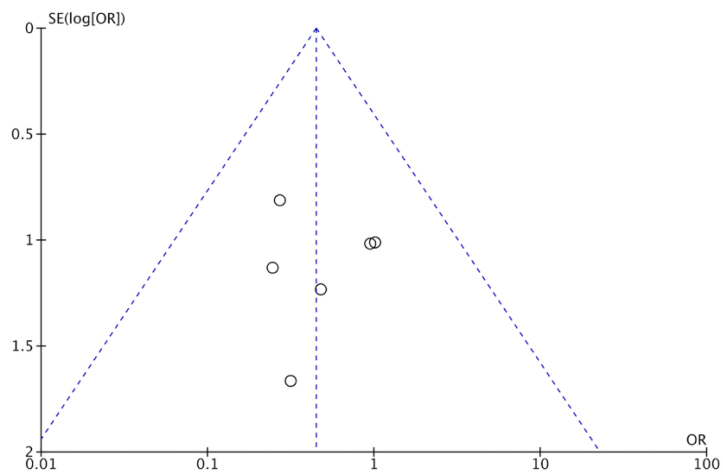
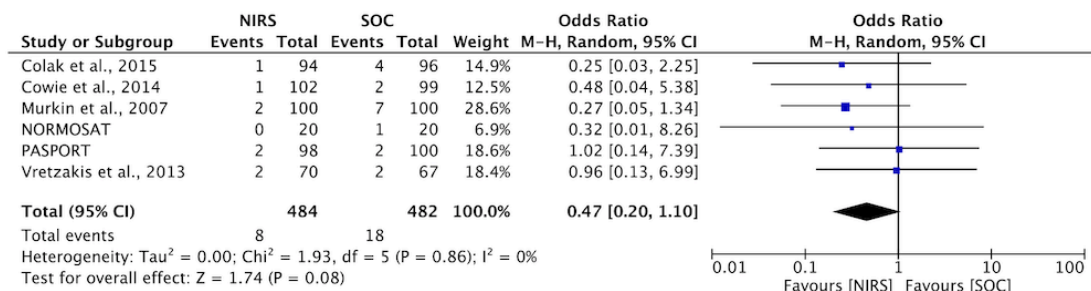


Figure S3. The effect of NIRS monitoring on MACEs. CI, confidence interval; MACE, major adverse cardiovascular event; M-H, Mantel-Haenszel test; NIRS, near-infrared spectroscopy; NORMOSAT, NORMAl cerebral Oxygen SATuration; PASPORT, PATient-Specific cerebral oxygenation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; SE, standard error; SOC, standard of care.

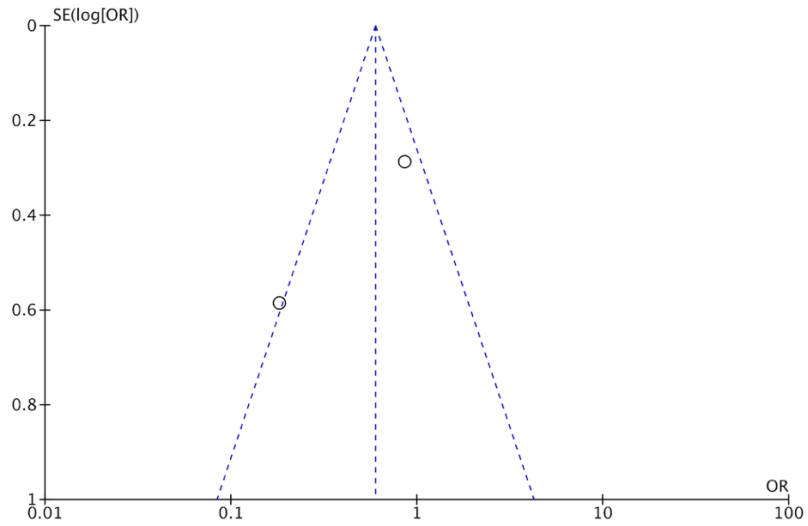
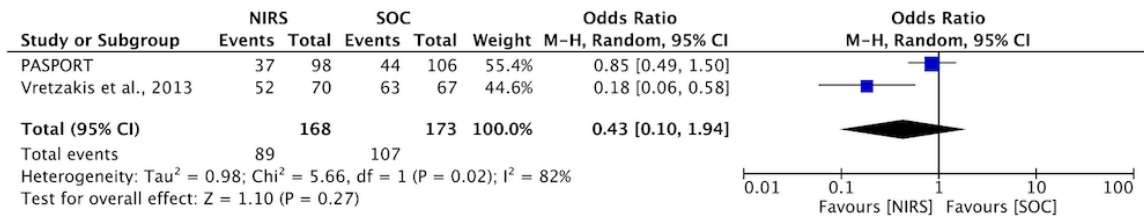


Figure S4. The effect of NIRS monitoring on bleeding/need for transfusions. CI, confidence interval; M-H, Mantel-Haenszel test; NIRS, near-infrared spectroscopy; PASPORT, PATient-Specific cerebral oxygenation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; SE, standard error; SOC, standard of care.

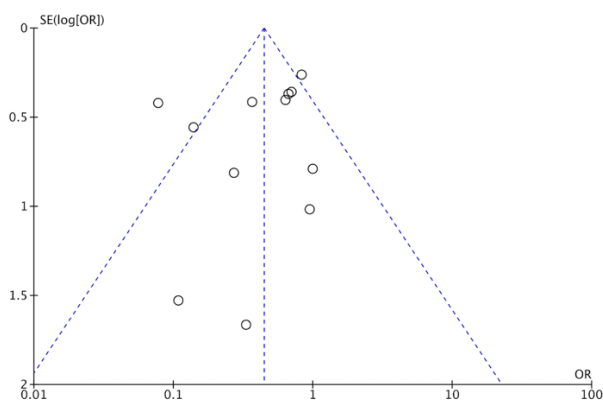
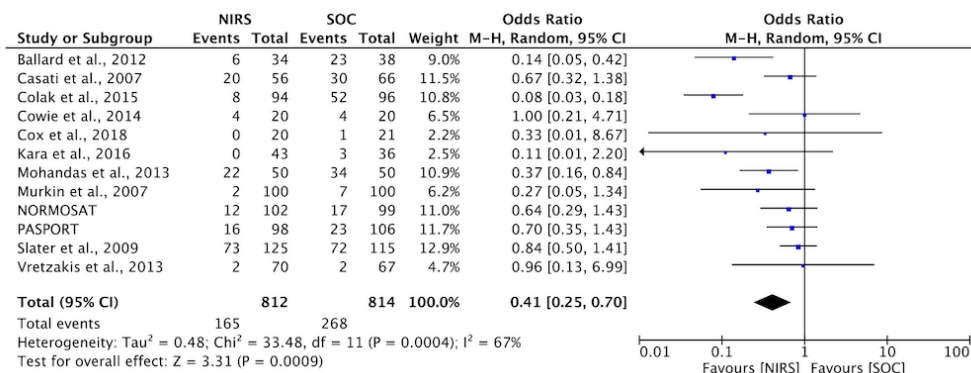


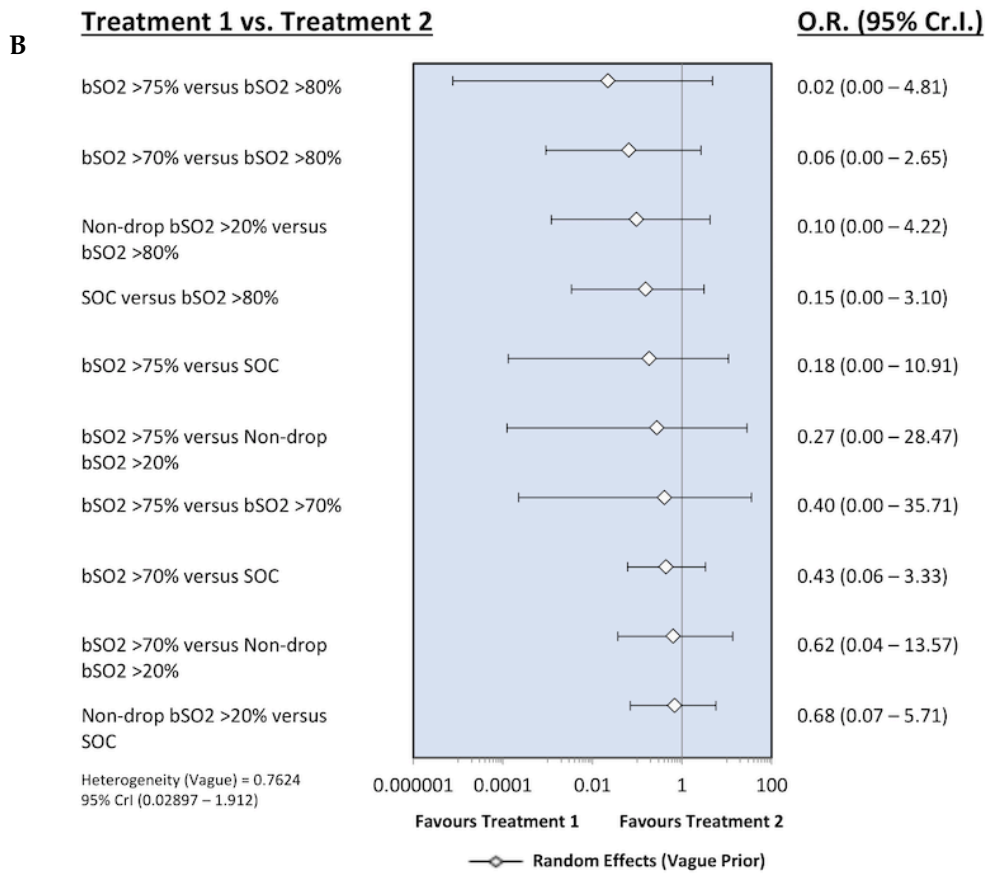
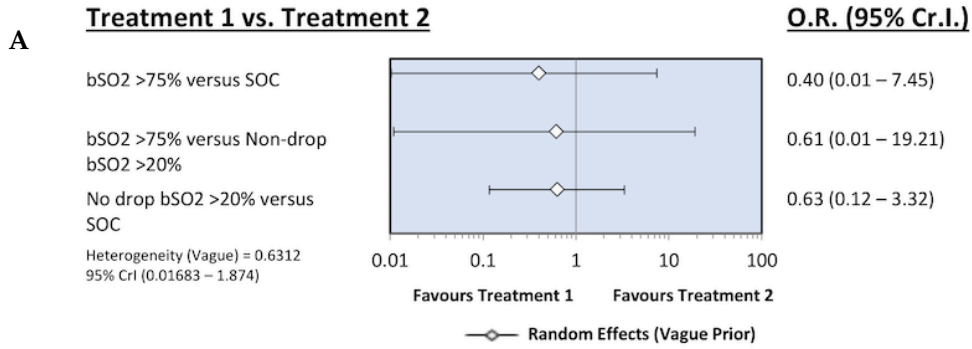
Figure S5. The effect of NIRS monitoring on morbidity combining POCD/POD, AKI and MACEs. CI, confidence interval; M-H, Mantel-Haenszel test; NIRS, near-infrared spectroscopy; NORMOSAT, NORMAl cerebral Oxygen SATuration; PASPORT, PATient-Specific cerebral oxygenation monitoring as Part Of an algorithm to Reduce Transfusion during heart valve surgery: a randomised controlled trial; SE, standard error; SOC, standard of care.

Table S4. The ranking of SUCRA assessable NIRS target values for three outcomes.

NIRS Target Values [†] INVOS and Non-INVOS Systems.	SUCRA [‡] Outcomes: A/B/C [§]
bSO ₂ > 75%	0.6717/0.5011/0.7696
bSO ₂ > 80%	NAs/0.8406/0.6852
bSO ₂ > 70%	NAs/0.4099/0.5514
Non-drop bSO ₂ > 20%	0.5623/0.3992/0.4073
SOC	0.2659/0.3492/0.0864

[§]The following outcomes providing numerical data were considered: (A) peri-/post-operative death, and (B) post-operative acute kidney function deterioration and (C) cardiovascular events occurrence.

[†] For both INVOS and non-INVOS system for monitoring, the NIRS target values presented were ranked according to probabilities for being the best, the second best, the third best, and so on $P(v = b)$, $b = 1, \dots, a$ following Markov chain Monte Carlo methods. [‡]SUCRA for each target value v out of the a competing target values requires calculation of the a vector of the cumulative probabilities $cum_{v,b}$ to be among the b best target value, $b = 1, \dots, a$. NAs, non-assessable; NIRS, near-infrared spectroscopy; SOC, standard or care; SUCRA, surface under the cumulative ranking area.



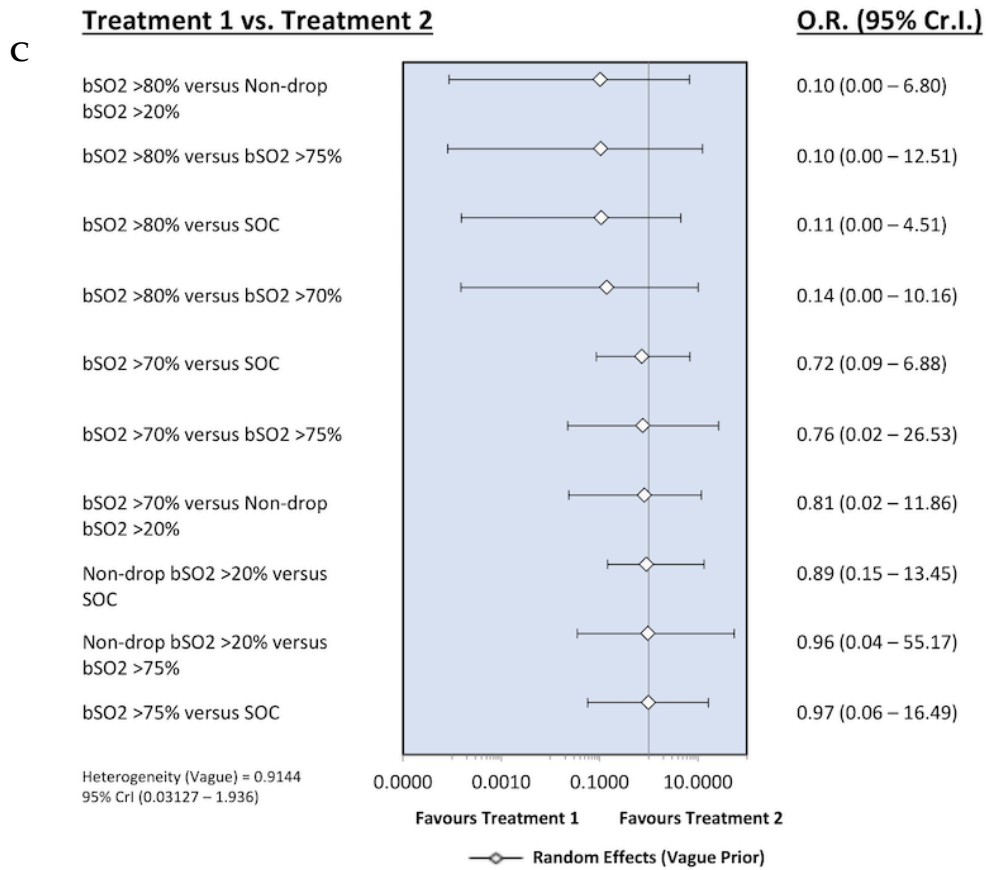
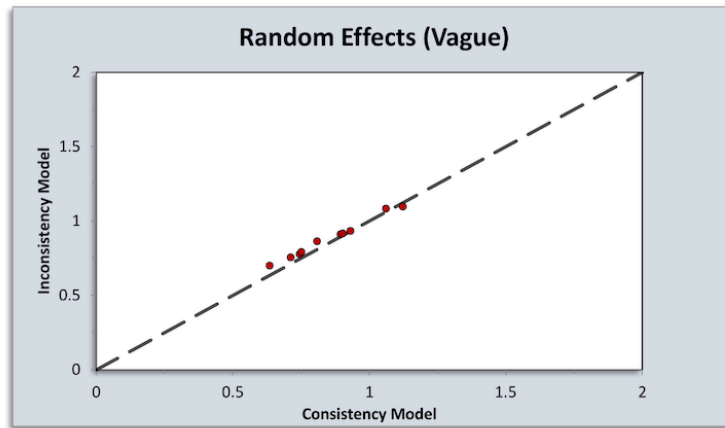
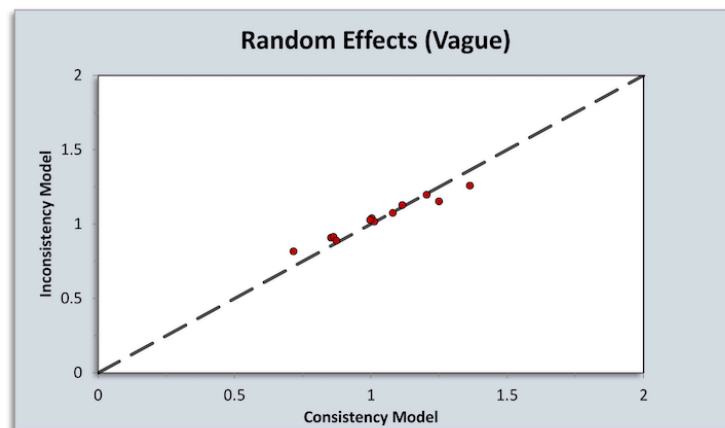


Figure S6. Network forests plot of the random effects (vague priors) for the SUCRA assessable NIRS target values corresponding to (A) post-operative death, (B) post-operative AKI, and (C) MACEs. CrI, credible intervals; OR, odds ratio; SOC, standard of care.

A



B



C

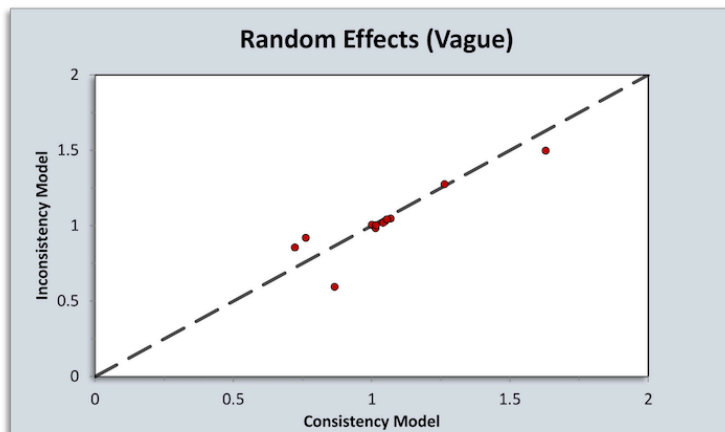


Figure S7. Inconsistency plot of the random effects for the SUCRA assessable NIRS target values corresponding to (A) post-operative death, (B) post-operative AKI, and (C) MACEs.

References

1. Colak, Z.; Borojevic, M.; Bogovic, A.; Ivancan, V.; Biocina, B.; Majeric-Kogler, V. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: A randomized, prospective study. *Eur. J. Cardiothorac. Surg.* **2015**, *47*, 447–454. <https://doi.org/10.1093/ejcts/ezu193>.
2. Deschamps, A.; Hall, R.; Grocott, H.; Mazer, C.D.; Choi, P.T.; Turgeon, A.F.; de Medicis, E.; Bussi eres, J.S.; Hudson, C.; Syed, S.; et al. Cerebral Oximetry Monitoring to Maintain Normal Cerebral Oxygen Saturation during High-risk Cardiac Surgery: A Randomized Controlled Feasibility Trial. *Anesthesiology* **2016**, *124*, 826–836. <https://doi.org/10.1097/ALN.0000000000001029>.
3. Kara, I.; Erkin, A.; Sacli, H.; Demirtas, M.; Percin, B.; Diler, M.S.; Kurali, K. The Effects of Near-Infrared Spectroscopy on the Neurocognitive Functions in the Patients Undergoing Coronary Artery Bypass Grafting with Asymptomatic Carotid Artery Disease: A Randomized Prospective Study. *Ann. Thorac. Cardiovasc. Surg.* **2015**, *21*, 544–550. <https://doi.org/10.5761/atcs.0a.15-00118>.
4. Mohandas, B.S.; Jagadeesh, A.M.; Vikram, S.B. Impact of monitoring cerebral oxygen saturation on the outcome of patients undergoing open heart surgery. *Ann. Card. Anaesth.* **2013**, *16*, 102–106. <https://doi.org/10.4103/0971-9784.109740>.
5. Slater, J.P.; Guarino, T.; Stack, J.; Vinod, K.; Bustami, R.T.; Brown III, J.M.; Rodriguez, A.L.; Magovern, C.J.; Zaubler, T.; Freundlich, K.; et al. Cerebral oxygen desaturation predicts cognitive decline and longer hospital stay after cardiac surgery. *Ann. Thorac. Surg.* **2009**, *87*, 36–45. <https://doi.org/10.1016/j.athoracsur.2008.08.070>.
6. Murkin, J.M.; Adams, S.J.; Novick, R.J.; Quantz, M.; Bainbridge, D.; Iglesias, I.; Cleland, A.; Schaefer, B.; Irwin, B.; Fox, S. Monitoring brain oxygen saturation during coronary bypass surgery: A randomized, prospective study. *Anesth. Analg.* **2007**, *104*, 51–58. <https://doi.org/10.1213/01.ane.0000246814.29362.f4>.
7. Vretzakis, G.; Georgopoulou, S.; Stamoulis, K.; Tassoudis, V.; Mikroulis, D.; Giannoukas, A.; Tsilimingas, N.; Karanikolas, M. Monitoring of brain oxygen saturation (INVOS) in a protocol to direct blood transfusions during cardiac surgery: A prospective randomized clinical trial. *J. Cardiothorac. Surg.* **2013**, *8*, 145. <https://doi.org/10.1186/1749-8090-8-145>.
8. Rogers, C.A.; Stoica, S.; Ellis, L.; Stokes, E.A.; Wordsworth, S.; Dabner, L.; Clayton, G.; Downes, R.; Nicholson, E.; Bennett, S.; et al. Randomized trial of near-infrared spectroscopy for personalized optimization of cerebral tissue oxygenation during cardiac surgery. *Br. J. Anaesth.* **2017**, *119*, 384–393. <https://doi.org/10.1093/bja/aex182>.
9. Cowie, D.A.; Nazareth, J.; Story, D.A. Cerebral oximetry to reduce perioperative morbidity. *Anaesth. Intensive Care* **2014**, *42*, 310–314. <https://doi.org/10.1177/0310057X1404200306>.
10. Ballard, C.; Jones, E.; Gauge, N.; Aarsland, D.; Nilsen, O.B.; Saxby, B.K.; Lowery, D.; Corbett, A.; Wesnes, K.; Katsaiti, E. Optimised anaesthesia to reduce post operative cognitive decline (POCD) in older patients undergoing elective surgery, a randomised controlled trial. *PLoS ONE* **2012**, *7*, e37410. <https://doi.org/10.1371/journal.pone.0037410>.
11. Casati, A.; Fanelli, G.; Pietropaoli, P.; Proietti, R.; Tufano, R.; Montanini, S. Monitoring cerebral oxygen saturation in elderly patients undergoing general abdominal surgery: A prospective cohort study. *Eur. J. Anaesthesiol.* **2007**, *24*, 59–65. <https://doi.org/10.1017/S0265021506001025>.
12. Cox, R.M.; Jamgochian, G.C.; Nicholson, K.; Wong, J.C.; Namdari, S.; Abboud, J.A. The effectiveness of cerebral oxygenation monitoring during arthroscopic shoulder surgery in the beach chair position: A randomized blinded study. *J. Shoulder Elbow Surg.* **2018**, *27*, 692–700. <https://doi.org/10.1016/j.jse.2017.11.004>.
13. Deschamps, A.; Lambert, J.; Couture, P.; Rochon, A.; Lebon, J.S.; Ayoub, C.; Cogan, J.; Denault, A. Reversal of decreases in cerebral saturation in high-risk cardiac surgery. *J. Cardiothorac. Vasc. Anesth.* **2013**, *27*, 1260–1266. <https://doi.org/10.1053/j.jvca.2013.01.019>.
14. Harilall, Y.; Adam, J.K.; Biccald, B.M.; Reddi, A. The effect of optimising cerebral tissue oxygen saturation on markers of neurological injury during coronary artery bypass graft surgery. *Heart Lung Circ.* **2014**, *23*, 68–74. <https://doi.org/10.1016/j.hlc.2013.07.002>.
15. Trafidło, T.; Gaszyński, T.; Gaszyński, W.; Nowakowska-Domagala, K. Intraoperative monitoring of cerebral NIRS oximetry leads to better postoperative cognitive performance: A pilot study. *Int. J. Surg.* **2015**, *16*, 23–30. <https://doi.org/10.1016/j.ijsu.2015.02.009>.