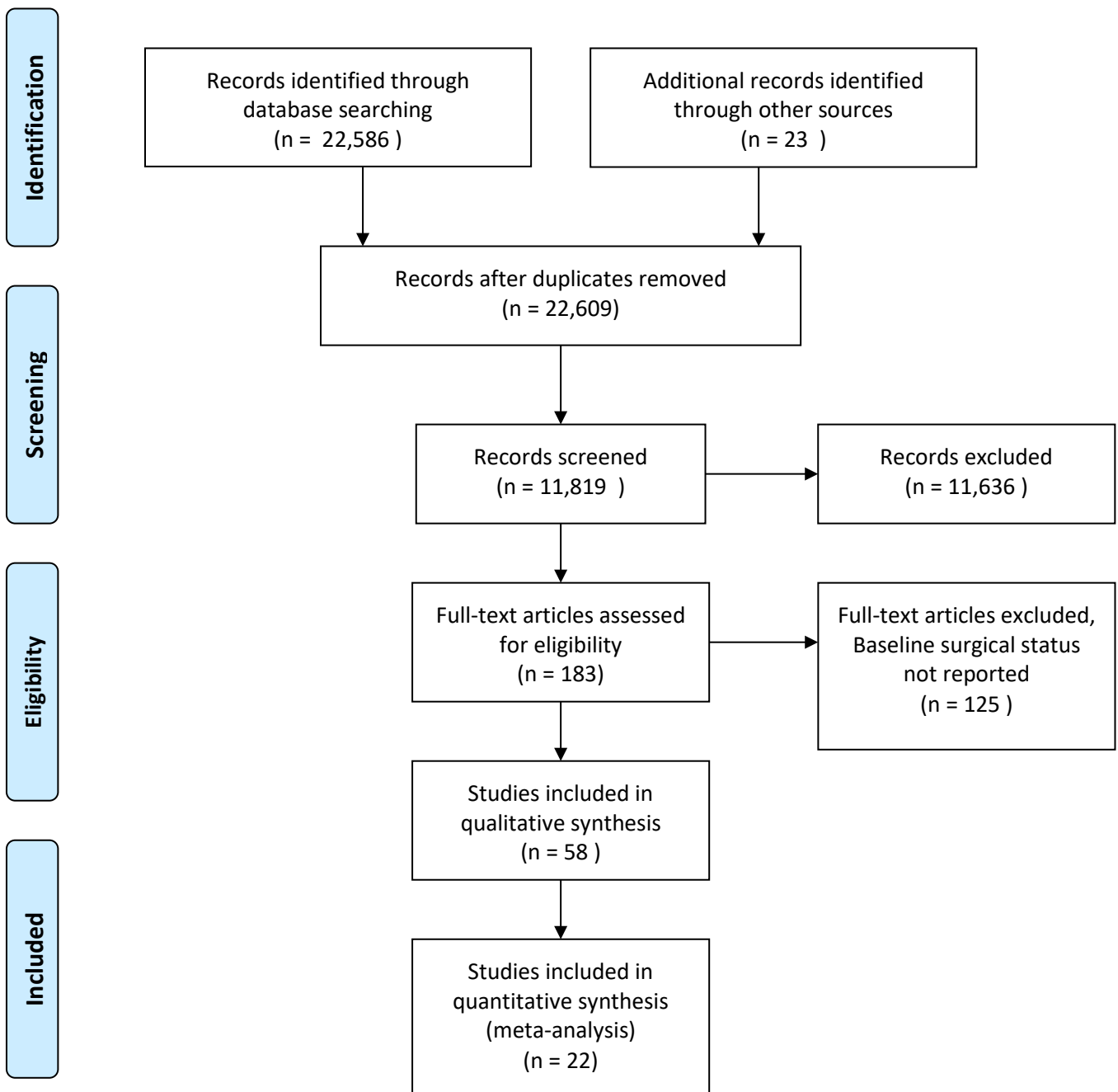


# **Baseline surgical status and short term mortality after ECMO for post-cardiotomy shock. Meta-analysis.**

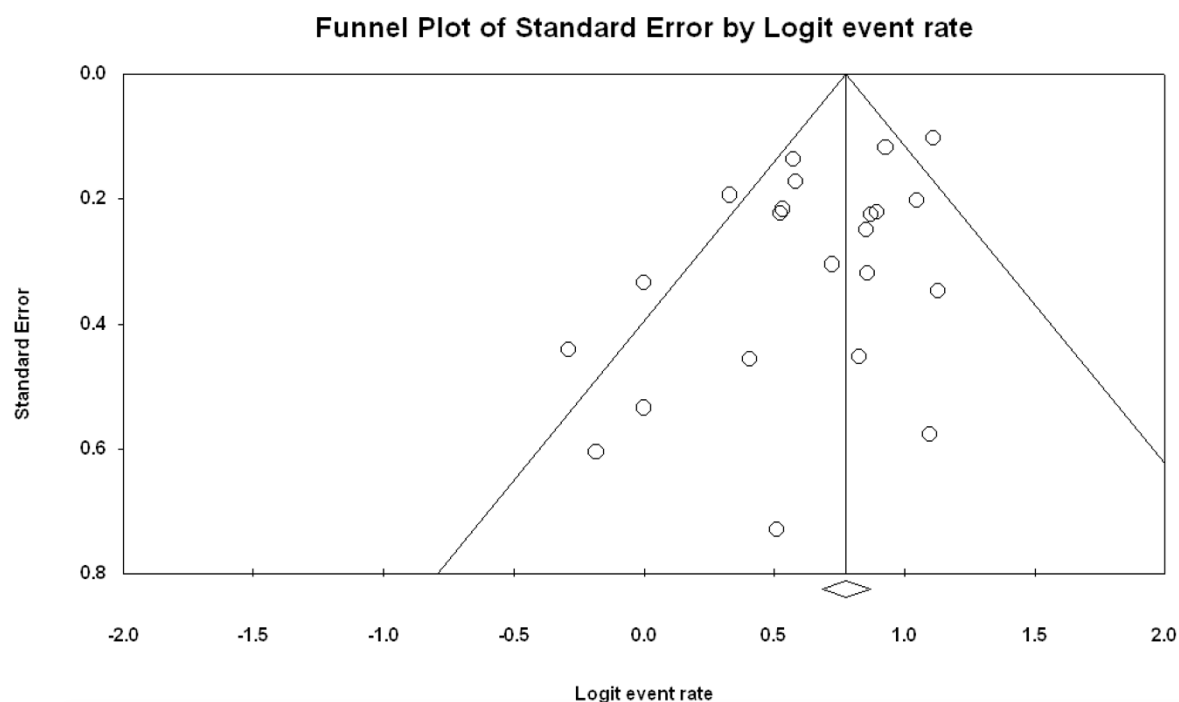
-ECMO for PCS depending on surgical status-

## **SUPPLEMENTARY APPENDIX**

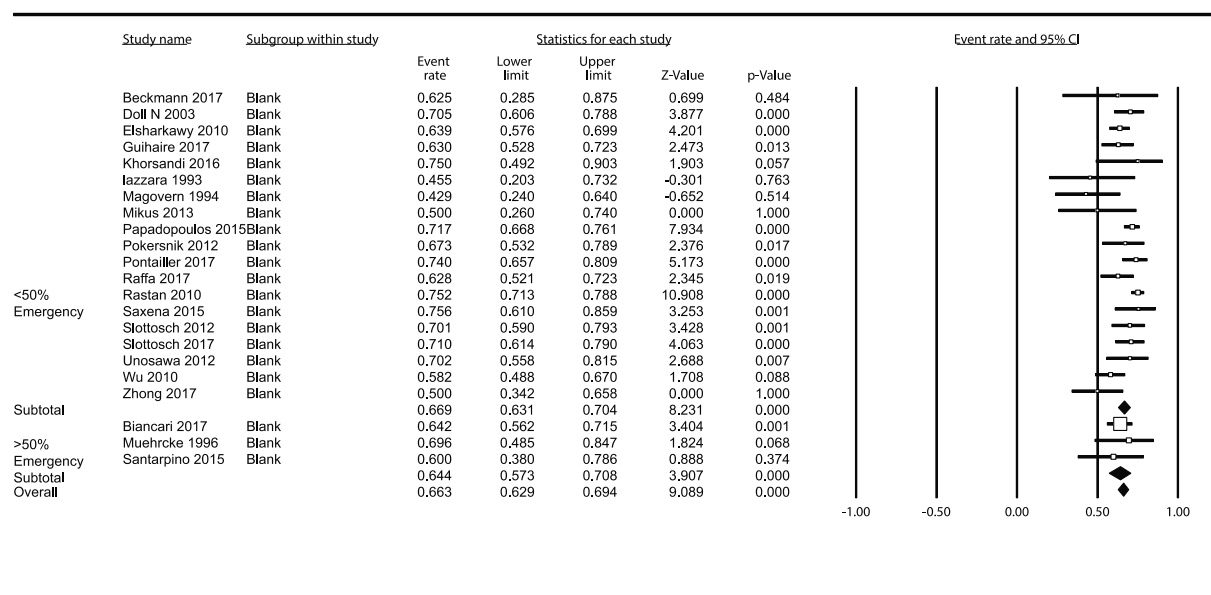
**Appendix Figure 1. PRISMA Flow Chart**



**Appendix Figure 2. Publication bias**

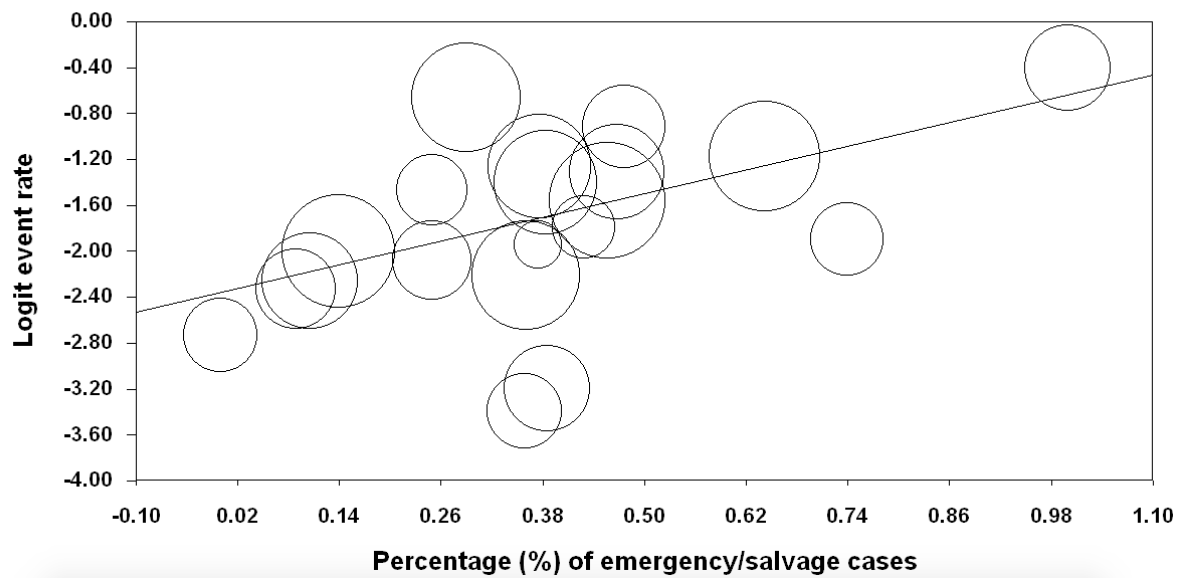


**Appendix Figure 3. Sensitivity analysis <50% emergency vs >50% emergency cases**



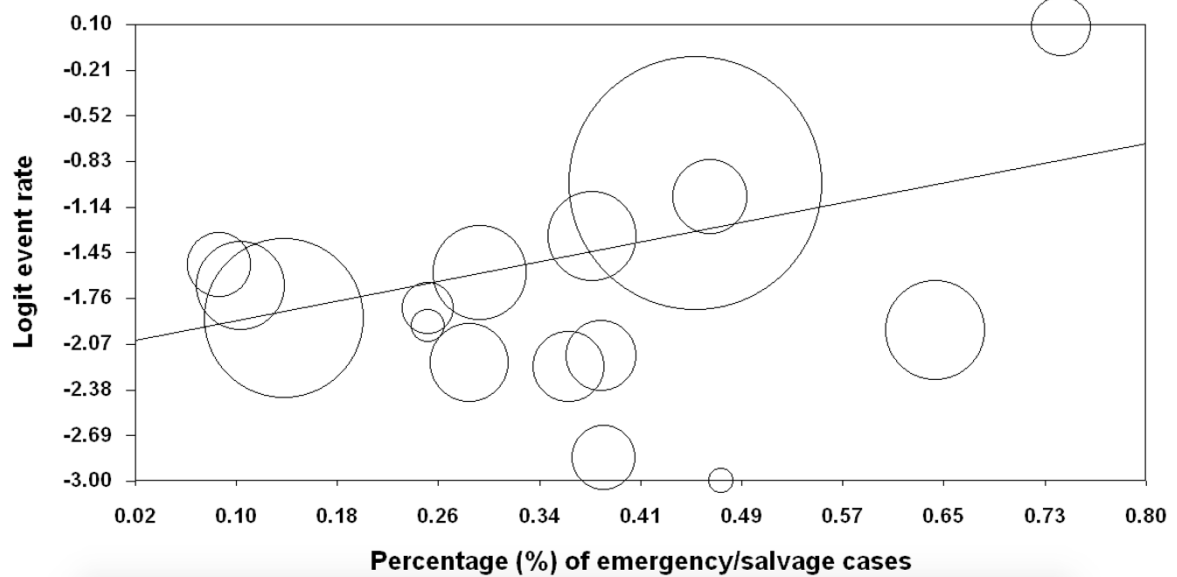
#### Appendix Figure 4. Neurologic complications

Regression of Percentage (%) of emergency/salvage cases on Logit event rate



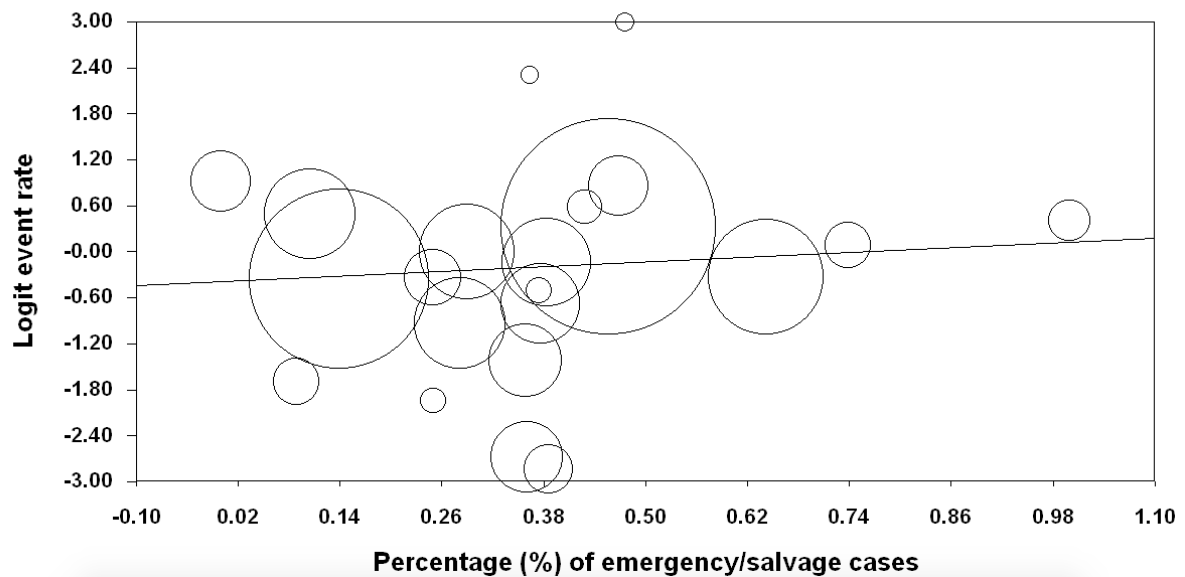
#### Appendix Figure 5. Limb complications

Regression of Percentage (%) of emergency/salvage cases on Logit event rate



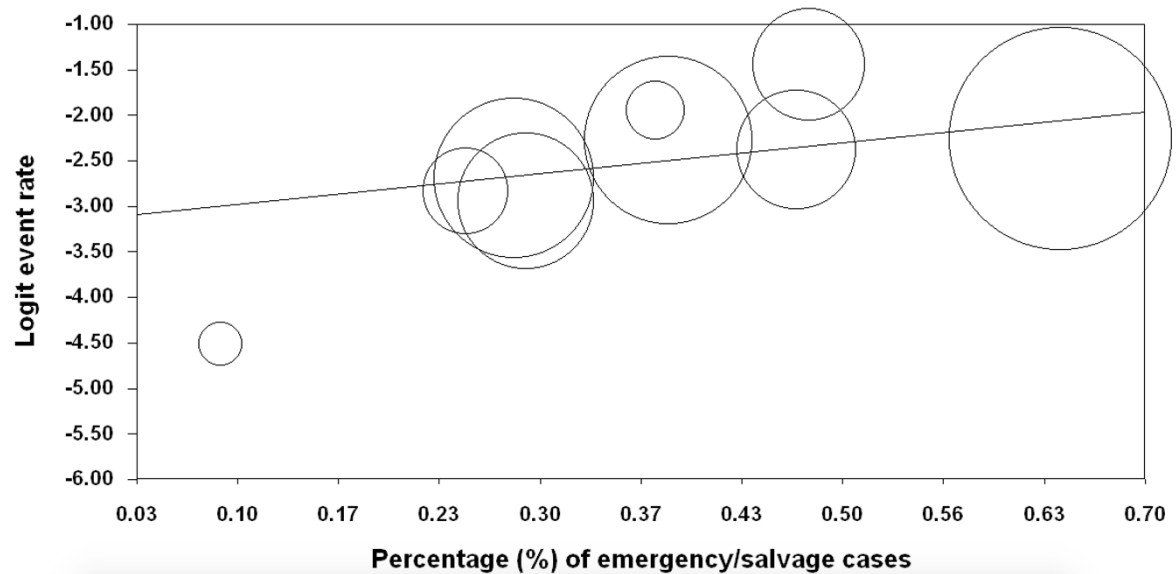
## Appendix Figure 6. Bleeding

Regression of Percentage (%) of emergency/salvage cases on Logit event rate



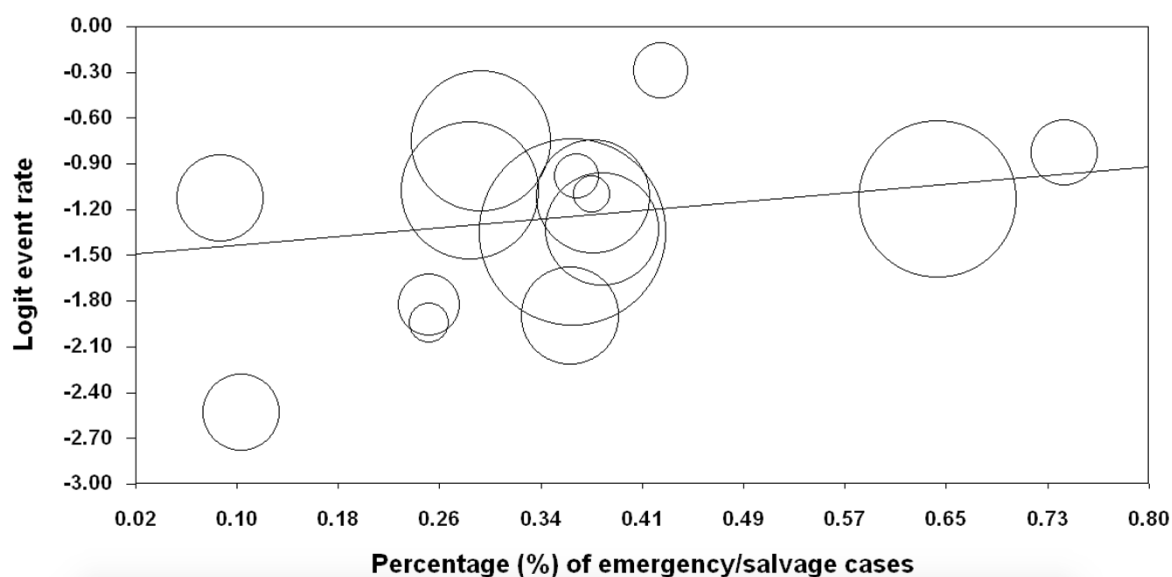
## Appendix Figure 7. Brain death

Regression of Percentage (%) of emergency/salvage cases on Logit event rate



## Appendix Figure 8. Sepsis

Regression of Percentage (%) of emergency/salvage cases on Logit event rate



## Appendix Figure 9. Cumulative analysis.

Study name	Statistics with study removed					Event rate (95% CI) with study removed				
	Point	Lower limit	Upper limit	Z-Value	p-Value					
Beckmann 2017	0.667	0.632	0.700	8.894	0.000					◆
Biancari 2017	0.668	0.632	0.702	8.621	0.000					◆
Doll N 2003	0.664	0.628	0.698	8.411	0.000					◆
Elsharkawy 2010	0.669	0.632	0.703	8.613	0.000					◆
Guihaire 2017	0.669	0.633	0.703	8.776	0.000					◆
Khorsandi 2016	0.665	0.630	0.698	8.778	0.000					◆
Iazzara 1993	0.670	0.636	0.702	9.300	0.000					◆
Magovern 1994	0.673	0.641	0.704	9.857	0.000					◆
Mikus 2013	0.670	0.636	0.702	9.226	0.000					◆
Muehrcke 1996	0.666	0.631	0.699	8.736	0.000					◆
Papadopoulos 2015	0.661	0.624	0.697	8.032	0.000					◆
Pokersnik 2012	0.666	0.630	0.700	8.642	0.000					◆
Pontallier 2017	0.662	0.626	0.696	8.395	0.000					◆
Raffa 2017	0.669	0.633	0.703	8.801	0.000					◆
Rastan 2010	0.660	0.628	0.690	9.339	0.000					◆
Santarpino 2015	0.668	0.633	0.701	8.940	0.000					◆
Saxena 2015	0.663	0.628	0.697	8.631	0.000					◆
Slottosch 2012	0.664	0.628	0.699	8.475	0.000					◆
Slottosch 2017	0.664	0.627	0.698	8.394	0.000					◆
Unosawa 2012	0.665	0.629	0.699	8.597	0.000					◆
Wu 2010	0.673	0.640	0.705	9.491	0.000					◆
Zhong 2017	0.674	0.641	0.705	9.746	0.000					◆
	0.667	0.633	0.699	9.032	0.000					◆

**Appendix Table 1. PRISMA CheckList**

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	7-8

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, Appendix
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Appendix
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10, Appendix
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-14



Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed10000

**Appendix Table 2.** ROBINS-I tool bias assessment.

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in measurement of interventions	Bias due to departures from	Bias due to missing data*	Bias in measurement of outcomes*	Bias in selection of reported result*	Overall bias	Cohen's Kappa
Beckmann 2017 [13]	Critical	Critical	Serious	NA	Low	Moderate	Moderate	Critical	71.4%
Biancari 2017 [14]	Critical	Low	Serious	NA	Low	Low	Low	Low	85.7%
Doll N 2003 [15]	Critical	Low	Low	NA	Moderate	Low	Low	Low	71.4%
Elsharkawy 2010 [16]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	85.7%
Guihaire 2017 [17]	Critical	Serious	Low	NA	Low	Moderate	Moderate	Moderate	85.7%
Khorsandi 2016 [18]	Critical	Low	Serious	NA	Low	Low	Low	Low	71.4%
Iazzara 1993 [19]	Critical	Low	Serious	NA	Moderate	Critical	Moderate	Moderate	71.4%
Magovern 1994 [20]	Critical	Low	Serious	NA	Moderate	Moderate	Critical	Moderate	71.4%
Mikus 2013 [21]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	85.7%
Muehrcke 1996 [22]	Critical	Moderate	Critical	NA	Serious	Low	Low	Moderate	85.7%
Papadopoulos 2015 [23]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	85.7%
Pokersnik 2012 [24]	Critical	Serious	Critical	NA	Low	Moderate	Moderate	Critical	71.4%
Pontailier 2017 [25]	Critical	Low	Serious	NA	Serious	Critical	Critical	Critical	71.4%
Raffa 2017 [26]	Critical	Low	Serious	NA	Low	Moderate	Low	Low	85.7%
Rastan 2010 [27]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	85.7%
Santarpino 2015 [28]	Critical	Low	Low	NA	Moderate	Low	Low	Low	71.4%
Saxena 2015 [29]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	71.4%
Slottosch 2012 [30]	Critical	Low	Low	NA	Low	Low	Moderate	Low	100%
Slottosch 2017 [31]	Critical	Low	Low	NA	Moderate	Moderate	Moderate	Moderate	71.4%
Unosawa 2012 [32]	Critical	Low	Low	NA	Low	Moderate	Moderate	Low	57.1%
Wu 2010 [33]	Critical	Low	Critical	NA	Low	Low	Low	Low	57.1%
Zhong 2017 [34]	Critical	Critical	Low	NA	Low	Serious	Moderate	Critical	71.4%

\*When multiple outcomes were reported for a study, the highest level of bias at the outcome level is reported in the table. Bias reported for comparison of peripheral vs central extracorporeal circulation and not for a study in general.

Appendix Table 3. Complications

Study (year) [reference]	Baseline status (elective/urgent/ emergency/salvage)	Neurological complications. N (%)	Brain death. N (%)	Limb complicatio ns. N (%)	AKI. N (%)	Sepsis. N (%)	Bleeding. N (%)	MOF. N (%)	Transfusions		
									RBC	FFP	PLT
Beckmann 2017 [e1]	NR/NR/3/NR	1 (12.5)	1 (12.5)	NR	4 (50.0)	2 (25.0)	3 (37.5)	1 (12.5)		NR	
Biancari 2017 [e2]	19/34/80/15	35 (23.6)	14 (9.5)	18 (12.2)	67 (45.3)	36 (24.3)	62 (41.9)	54 (36.5)	17±17	14±21	28±72
Doll N 2003 [e3]	21/64/10/0	9 (9.5)	NR	15 (15.8)	64 (67.4)	7 (7.4)	59 (62.1)	12 (12.6)	30±20		NR
Elsharkawy 2010 [e4]	NR/NR/84/NR	23 (9.9)	NR	NR	101 (43.3)	48 (20.6)	15 (6.4)	75 (32.2)		NR	
Guihaire 2017 [e5]	NR/NR/33/NR	3 (3.3)	NR	9 (9.8)	NR	12 (12.6)	18 (19.6)	41 (70.7)	12±1		NR
Khorsandi 2016 [e6]*	9/3/4/0	3 (18.8)	NR	2 (12.5)	3 (18.8)	2 (12.5)	2 (12.5)	1 (6.3)		NR	
Iazzara 1993 [e7]	1/6/4/0	NR	NR	NR	1 (9.1)	3 (27.3)	10 (90.9)	5 (45.5)	25±9	21±7	41±10
Magovern 1994 [e8]	0/11/10/0	6 (28.6)	4 (19.0)	1 (4.8)	1 (4.8)	NR	20 (95.2)	NR	28±5	21±7	40±15
Mikus 2013 [e9]	6/2/6/0	2 (14.3)	NR	NR	7 (50.0)	6 (42.9)	9 (64.3)	6 (42.9)	54±36	NR	18±9
Muehrcke 1996 [e10]	6/0/17/0	3 (13.0)	NR	12 (52.2)	12 (52.2)	7 (30.4)	12 (52.2)	5 (21.7)	43±22	10±12	59±40
Papadopoulos 2015 [e11]	NR/NR/NR/50	43 (11.9)	NR	47 (13.1)	220 (61.1)	NR	148 (41.1)	248 (69.0)		NR	
Pokersnik 2012 [e12]	NR/NR/0/0	3 (6.1)	NR	NR	16 (32.7)	NR	35 (71.4)	NR		NR	
Pontailier 2017 [e13]*	NR/NR/49/NR	5 (3.9)	NR	7 (5.5)	NR	NR	7 (5.5)	NR	4±5	1±1	3±4
Raffa 2017 [e14]	NR/NR/33/NR	17 (19.8)	8 (9.3)	9 (10.5)	26 (30.2)	18 (20.9)	40 (46.5)	NR		NR	
Rastan 2010 [e15]	159/122/205/31	90 (17.4)	NR	141 (27.3)	336 (65.0)	NR	300 (58.0)	NR	14±12	14±13	2±NR
Santarpino 2015 [e16]	0/0/0/20	8 (40.0)	NR	NR	7 (35.0)	NR	12 (60.0)	NR	80%	54%	43%
Saxena 2015 [e17]	35/6/4/0	4 (8.9)	0	8 (17.8)	20 (44.4)	11 (24.4)	7 (15.6)	13 (38.2)		NR	
Slottosch 2012 [e18]	NR/NR/29/NR	17 (22.1)	NR	16 (20.8)	53 (68.8)	19 (24.7)	26 (33.8)	NR	29±16	18±13	4±3
Slottosch 2017 [e19]*	NR/NR/37/0	34 (24.5)	5 (3.6)	17 (12.2)	92 (66.2)	32 (23.0)	50 (36.0)	NR	38±12	21±22	5±6
Unosawa 2012 [e20]	NR/NR/22/NR	10 (21.3)	4 (8.5)	12 (25.5)	15 (31.9)	NR	33 (70.2)	18 (38.3)		NR	
Wu 2010 [e21]	NR/NR/31/NR	NR	7 (6.4)	11 (10.0)	46 (41.8)	28 (25.5)	31 (28.2)	28 (25.5)		NR	
Zhong 2017 [e22]	NR/NR/9/NR	4 (11.1)	2 (5.6)	5 (13.9)	NR	5 (13.9)	15 (41.7)	7 (19.4)	13±10	10±4	2±1
Regression complication rate (%) vs emergency/non-emergency ratio: coefficient and p-value		$\beta_{\text{coef}} =$ <b>1.721</b> $P_{\text{slope}} =$ <b>&lt; 0.001</b>	$\beta_{\text{coef}} =$ 1.958 $P_{\text{slope}} =$ 0.099	$\beta_{\text{coef}} =$ <b>1.711</b> $P_{\text{slope}} <$ <b>0.001</b>	$\beta_{\text{coef}} =$ - 0.428 $P_{\text{slope}} =$ 0.526	$\beta_{\text{coef}} =$ - 0.732 $P_{\text{slope}} =$ 0.134	$\beta_{\text{coef}} =$ - <b>0.507</b> $P_{\text{slope}} =$ <b>0.051</b>	$\beta_{\text{coef}} =$ - 0.201 $P_{\text{slope}} =$ 0.886		NA	

\* Reported for entire study population including non-PCS patients

AKI, acute kidney injury; RBC, redo blood cells; FFP, fresh frozen plasma; PLT, platelets; MOF, multi-organ failure; NR, not reported

## Supplementary references:

1. Beckmann E, Ismail I, Cebotari S, Busse A, Martens A, Shrestha M, Kuhn C, Haverich A, Fegbeutel C. Right-sided heart failure and extracorporeal life support in patients undergoing pericardiectomy for constrictive pericarditis: A risk factor analysis for adverse outcome. *Thorac Cardiovasc Surg*. 2017;65:662-670
2. Biancari F, Dalen M, Perrotti A, Fiore A, Reichart D, Khodabandeh S, Gulbins H, Zipfel S, Al Shakaki M, Welp H, Vezzani A, Gherli T, Lommi J, Juvonen T, Svenarud P, Chocron S, Verhoye JP, Bounader K, Gatti G, Gabrielli M, Saccocci M, Kinnunen EM, Onorati F, Santarpino G, Alkhamees K, Ruggieri VG, Dell'Aquila AM. Venoarterial extracorporeal membrane oxygenation after coronary artery bypass grafting: Results of a multicenter study. *Int J Cardiol*. 2017;241:109-114
3. Doll N, Fabricius A, Borger MA, Bucerius J, Doll S, Kramer K, Ullmann C, Schmitt DV, Walther T, Falk V, Mohr FW. Temporary extracorporeal membrane oxygenation in patients with refractory postoperative cardiogenic shock--a single center experience. *J Card Surg*. 2003;18:512-518
4. Elsharkawy HA, Li L, Esa WA, Sessler DI, Bashour CA. Outcome in patients who require venoarterial extracorporeal membrane oxygenation support after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24:946-951
5. Guihaire J, Dang Van S, Rouze S, Rosier S, Roisne A, Langanay T, Corbineau H, Verhoye JP, Flecher E. Clinical outcomes in patients after extracorporeal membrane oxygenation support for post-cardiotomy cardiogenic shock: A single-centre experience of 92 cases. *Interact Cardiovasc Thorac Surg*. 2017;25:363-369
6. Khorsandi M, Shaikhrezai K, Prasad S, Pessotto R, Walker W, Berg G, Zamvar V. Advanced mechanical circulatory support for post-cardiotomy cardiogenic shock: A 20-year outcome analysis in a non-transplant unit. *J Cardiothorac Surg*. 2016;11:29
7. Lazzara RR, Magovern JA, Benckart DH, Maher TD, Jr., Sakert T, Magovern GJ, Jr. Extracorporeal membrane oxygenation for adult post cardiotomy cardiogenic shock using a heparin bonded system. *ASAIO J*. 1993;39:M444-447

8. Magovern GJ, Jr., Magovern JA, Benckart DH, Lazzara RR, Sakert T, Maher TD, Jr., Clark RE. Extracorporeal membrane oxygenation: Preliminary results in patients with postcardiotomy cardiogenic shock. *Ann Thorac Surg.* 1994;57:1462-1468; discussion 1469-1471
9. Mikus E, Tripodi A, Calvi S, Giglio MD, Cavallucci A, Lamarra M. Centrimag venoarterial extracorporeal membrane oxygenation support as treatment for patients with refractory postcardiotomy cardiogenic shock. *ASAIO J.* 2013;59:18-23
10. Muehrcke DD, McCarthy PM, Stewart RW, Foster RC, Ogella DA, Borsh JA, Cosgrove DM, 3rd. Extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock. *Ann Thorac Surg.* 1996;61:684-691
11. Papadopoulos N, Marinos S, El-Sayed Ahmad A, Keller H, Meybohm P, Zacharowski K, Moritz A, Zierer A. Risk factors associated with adverse outcome following extracorporeal life support: Analysis from 360 consecutive patients. *Perfusion.* 2015;30:284-290
12. Pokersnik JA, Buda T, Bashour CA, Gonzalez-Stawinski GV. Have changes in ecmo technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? *J Card Surg.* 2012;27:246-252
13. Pontailler M, Demondion P, Lebreton G, Golmard JL, Leprince P. Experience with extracorporeal life support for cardiogenic shock in the older population more than 70 years of age. *ASAIO J.* 2017;63:279-284
14. Raffa GM, Gelsomino S, Sluijpers N, Meani P, Alenizy K, Natour E, Bidar E, Johnson DM, Makhoul M, Heuts S, Lozekoot P, Kats S, Schreurs R, Delnoij T, Montalti A, Sels JW, Poll MV, Roekaerts P, Maessen J, Lorusso R. In-hospital outcome of post-cardiotomy extracorporeal life support in adult patients: The 2007-2017 maastricht experience. *Crit Care Resusc.* 2017;19:53-61
15. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T, Mohr FW. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg.* 2010;139:302-311, 311 e301
16. Santarpino G, Ruggieri VG, Mariscalco G, Bounader K, Beghi C, Fischlein T, Onorati F, Faggian G, Gatti G, Pappalardo A, De Feo M, Bancone C, Perrotti A, Chocron S, Dalen M, Svenarud P, Rubino AS, Mignosa C, Gherli R, Musumeci F, Dell'Aquila AM, Kinnunen EM, Biancari F.

Outcome in patients having salvage coronary artery bypass grafting. *Am J Cardiol*.

2015;116:1193-1198

17. Saxena P, Neal J, Joyce LD, Greason KL, Schaff HV, Guru P, Shi WY, Burkhart H, Li Z, Oliver WC, Pike RB, Haile DT, Schears GJ. Extracorporeal membrane oxygenation support in postcardiotomy elderly patients: The mayo clinic experience. *Ann Thorac Surg*. 2015;99:2053-2060
18. Slottosch I, Liakopoulos O, Kuhn E, Deppe AC, Scherner M, Madershahian N, Choi YH, Wahlers T. Outcomes after peripheral extracorporeal membrane oxygenation therapy for postcardiotomy cardiogenic shock: A single-center experience. *J Surg Res*. 2013;181:e47-55
19. Slottosch I, Liakopoulos O, Kuhn E, Scherner M, Deppe AC, Sabashnikov A, Mader N, Choi YH, Wippermann J, Wahlers T. Lactate and lactate clearance as valuable tool to evaluate ecmo therapy in cardiogenic shock. *J Crit Care*. 2017;42:35-41
20. Unosawa S, Sezai A, Hata M, Nakata K, Yoshitake I, Wakui S, Kimura H, Takahashi K, Hata H, Shiono M. Long-term outcomes of patients undergoing extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *Surg Today*. 2013;43:264-270
21. Wu MY, Lin PJ, Lee MY, Tsai FC, Chu JJ, Chang YS, Haung YK, Liu KS. Using extracorporeal life support to resuscitate adult postcardiotomy cardiogenic shock: Treatment strategies and predictors of short-term and midterm survival. *Resuscitation*. 2010;81:1111-1116
22. Zhong Z, Jiang C, Yang F, Hao X, Xing J, Wang H, Hou X. Veno-arterial extracorporeal membrane oxygenation support in patients undergoing aortic surgery. *Artif Organs*. 2017;41:1113-1120
23. Hervey-Jumper SL, Annich GM, Yancon AR et al. Neurological complications of extracorporeal membrane oxygenation in children. *J Neurosurg Pediatr*. 2011;7:338-344
24. Jayaraman AL, Cormican D, Shah P, et al. Cannulation strategies in adult veno-arterial and veno-venous extracorporeal membrane oxygenation: Techniques, limitations, and special considerations. *Ann Card Anaesth*. 2017;20:S11-S18
25. Takayama H, Landes E, Truby L et al. Feasibility of smaller arterial cannulas in venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2015;149:1428-1433

