What meta-analyses of recent trials of ECPR tell us…

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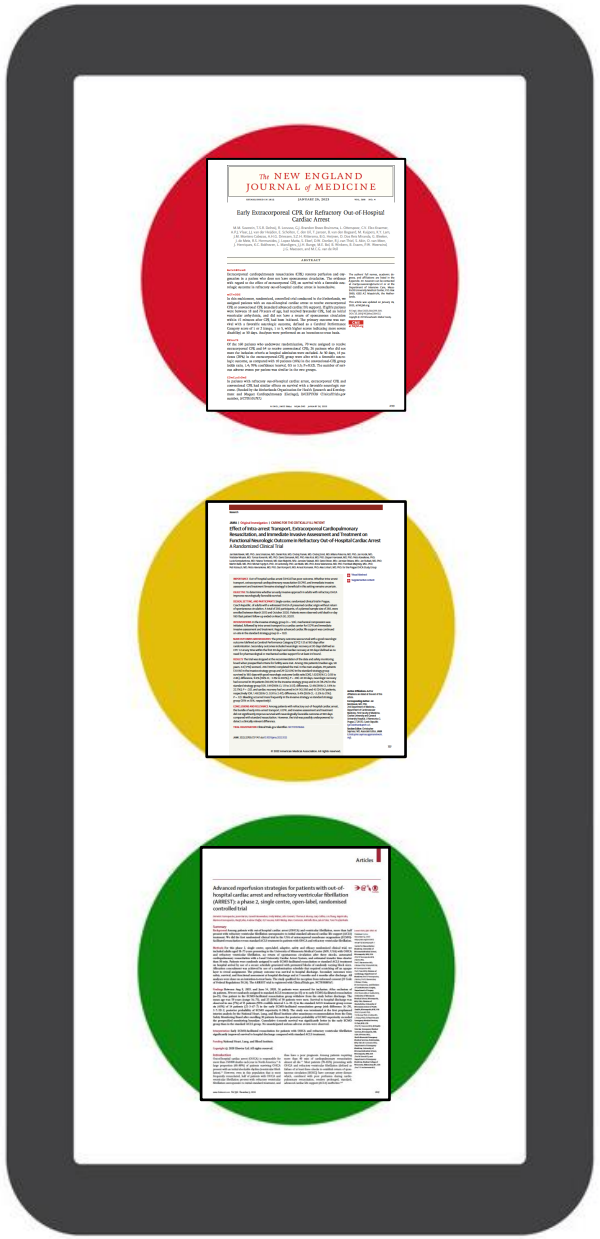
Disclosures

Getinge

Research funding



INCEPTION trial

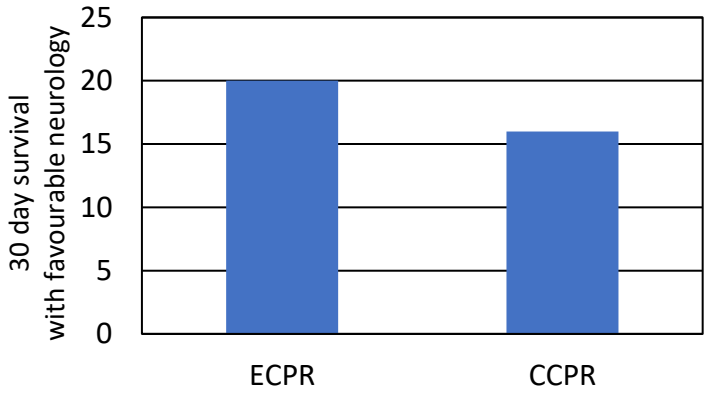
N Engl J Med 2023;388:299-309

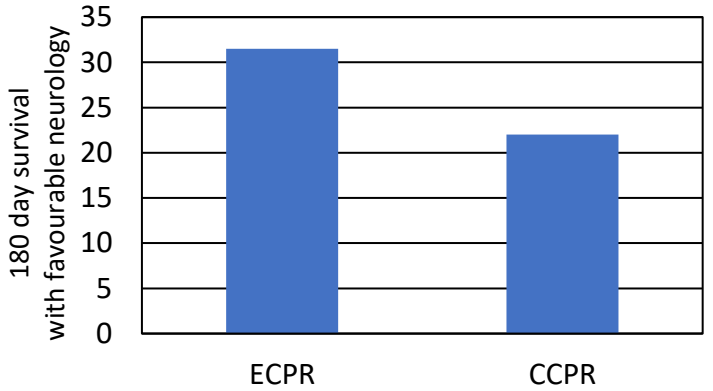
Prague OHCA study

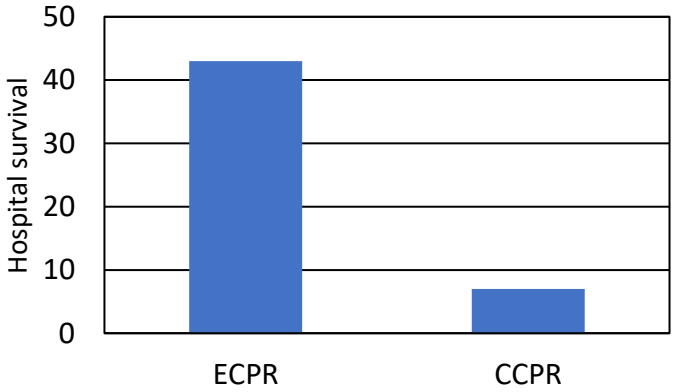
JAMA 2022;327:737-747

ARREST trial

Lancet 2020;396:1807-16







EMERGENCY MEDICAL SERVICES/ORIGINAL RESEARCH

Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest (EROCA): Results of a Randomized Feasibility Trial of Expedited Out-of-Hospital Transport

Cindy H. Hsu, MD, PhD*; William J. Meurer, MD, MS; Robert Domeier, MD; Jennifer Fowler, RN; Sage P. Whitmore, MD; Benjamin S. Bassin, MD; Kyle J. Gunnerson, MD; Jonathan W. Haft, MD; William R. Lynch, MD; Brahmajee K. Nallamothu, MD, MPH; Renee A. Havey, RN; Kelley M. Kidwell, PhD; William C. Stacey, MD, PhD; Robert Silbergleit, MD; Robert H. Bartlett, MD; Robert W. Neumar, MD, PhD

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Study objective: Outcomes of extracorporeal cardiopulmonary resuscitation (ECPR) for out-of-hospital cardiac arrest depend on time to therapy initiation. We hypothesize that it would be feasible to select refractory out-of-hospital cardiac arrest patients for expedited transport based on real-time estimates of the 911 call to the emergency department (ED) arrival interval, and for emergency physicians to rapidly initiate ECPR in eligible patients.

Methods: In a 2-tiered emergency medical service with an ECPR-capable primary destination hospital, adults with refractory shockable or witnessed out-of-hospital cardiac arrest were randomized 4:1 to expedited transport or standard care if the predicted 911 call to ED arrival interval was less than or equal to 30 minutes. The primary outcomes were the proportion of subjects with 911 call to ED arrival less than or equal to 30 minutes and ED arrival to ECPR flow less than or equal to 30 minutes.

Results: Of 151 out-of-hospital cardiac arrest 911 calls, 15 subjects (10%) were enrolled. Five of 12 subjects randomized to expedited transport had an ED arrival time of less than or equal to 30 minutes (overall mean 32.5 minutes [SD 7.1]), and 5 were eligible for and treated with ECPR. Three of 5 ECPR-treated subjects had flow initiated in less than or equal to 30 minutes of ED arrival (overall mean 32.4 minutes [SD 10.9]). No subject in either group survived with a good neurologic outcome.

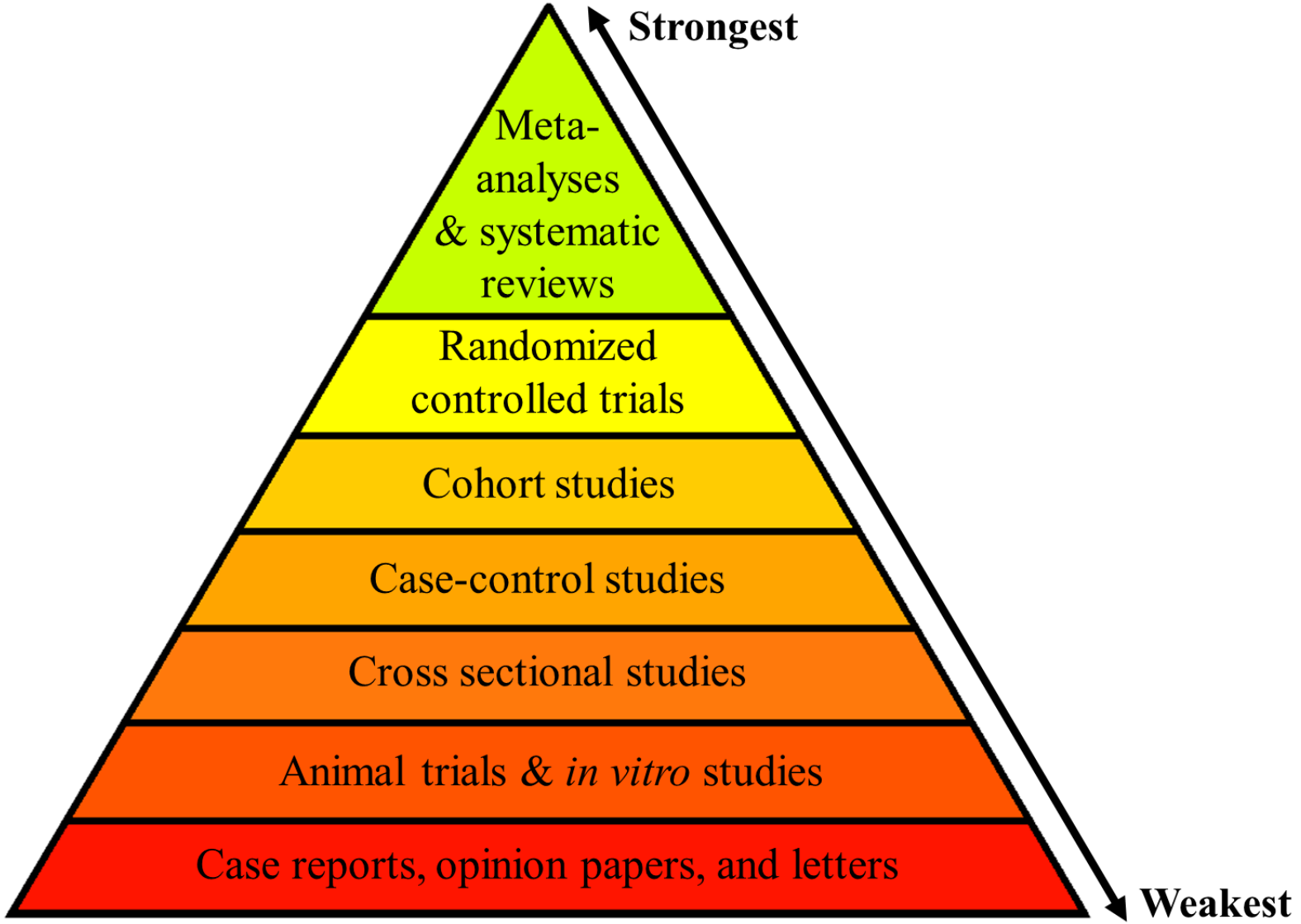
Conclusion: The Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest trial did not meet predefined feasibility outcomes for selecting out-of-hospital cardiac arrest patients for expedited transport and initiating ECPR in the ED. Additional research is needed to improve the accuracy of predicting the 911 call to ED arrival interval, optimize patient selection, and reduce the ED arrival to ECPR flow interval. [Ann Emerg Med. 2021;78:92-101.]

Please see page 93 for the Editor's Capsule Summary of this article.

- Study design
  - Transport + ECPR vs. CCPR on site
  - 4:1 randomization
- Enrolled
  - 12:3 (5/12 received ECPR)
  - Early termination (low recruitment)
- Outcomes
  - ECPR-group 0/12 survivors
  - CCPR-group 1/3 survivor@90 days (CPC3)

Hsu et al. Ann Emerg Med 2021;78:92-101

Hierarchy of Scientific Evidence



Search	Actions	Details	Query	Results	Time
#1	•••	›	Search: **extracorporeal cardiopulmonary resuscitation** Filters: **Meta-Analysis, from 2023/1/26 - 3000/12/12** Sort by: **Publication Date**	18	11:03:22

- **8 meta-analyses**
  - **5 meta-analyses of randomized controlled trials**
  - **1 meta-analysis of randomized controlled trials + matched cohorts**
  - **1 update of abovementioned meta-analysis**
  - **1 meta-analysis of matched cohorts**

5 meta-analyses of randomized controlled trials

ECPR was associated with a ***significant improvement in short-term favorable neurological outcomes*** compared with CCPR

Kiyohara et al. J Cardiovasc Med (Hagerstown). 2023 Jul 1;24(7):414-419

Extracorporeal CPR compared with conventional CPR ***increased survival with favorable neurological outcome*** in adults with refractory out-of-hospital cardiac arrest, especially when the initial rhythm was shockable.

Scquizatto et al. Artif Organs. 2023 May;47(5):806-816

The current randomized data ***do not provide solid evidence for*** the routine application of ECPR in patients with refractory OHCA.

Ali et al. JACC Cardiovasc Interv. 2023 Jul 24;16(14):1825-1827

ECPR was ***not associated with a significant improvement in survival*** with favorable neurologic outcomes in refractory OHCA patients.

Gomes et al. Intern Emerg Med. 2023 Oct;18(7):2113-2120

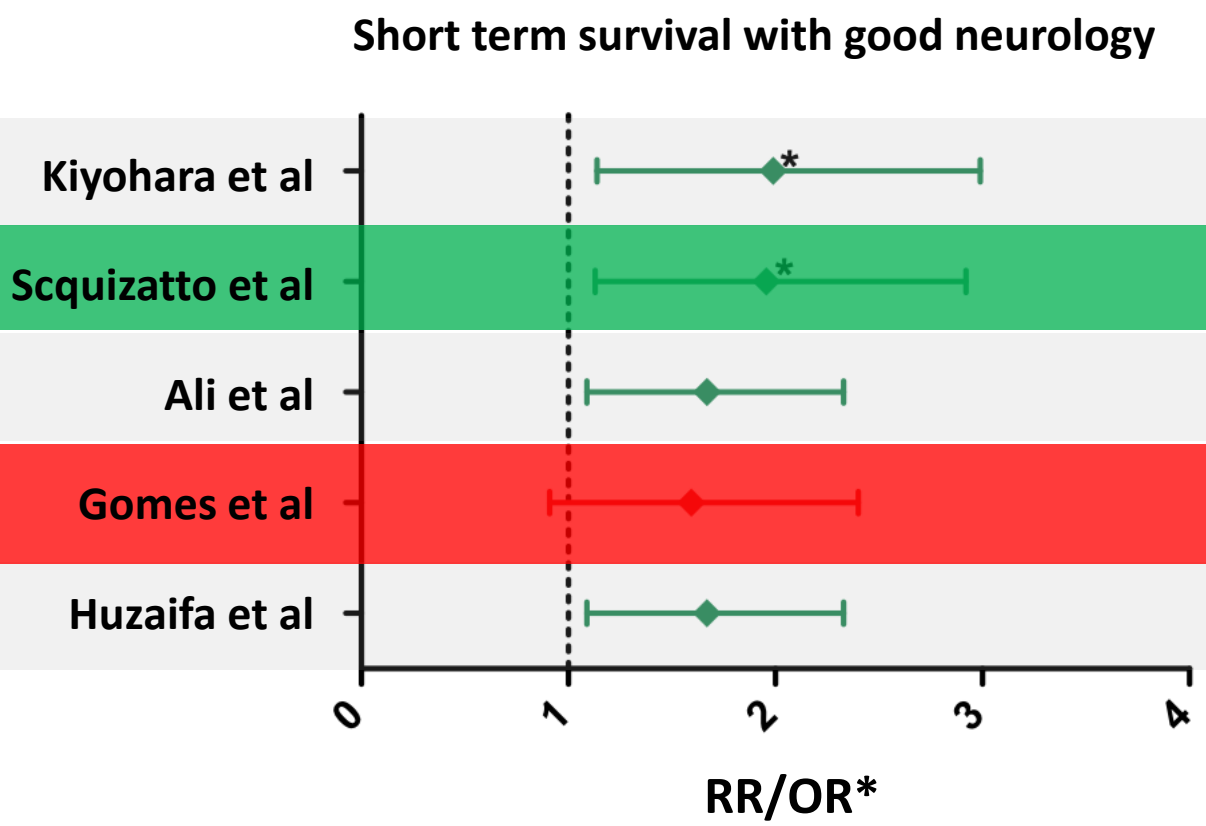
ECPR in OHCA patients was ***not associated with improved survival*** or long-term favorable neurological outcome but ***did improve favorable neurological outcome in the mid-term.***

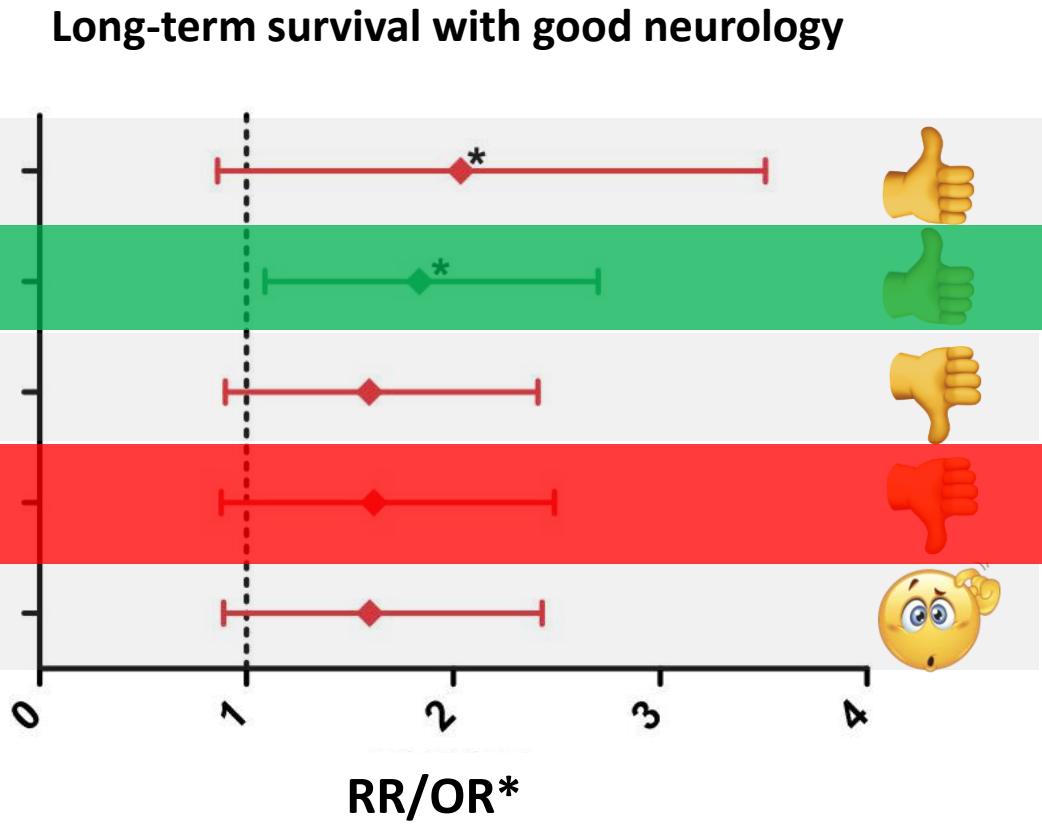
Huzaifa et al. Pacing Clin Electrophysiol. 2023 Oct;46(10):1246-1250

Discrepancies between these analyses

- With (3/5) or without (2/5) EROCA trial
- Random effects (2/5) vs fixed effect (1/5)
  - 2/5 not reported
- Outcome definitions
  - Short term: 30 days, hospital mortality
  - Long term: 6 months, longest follow-up

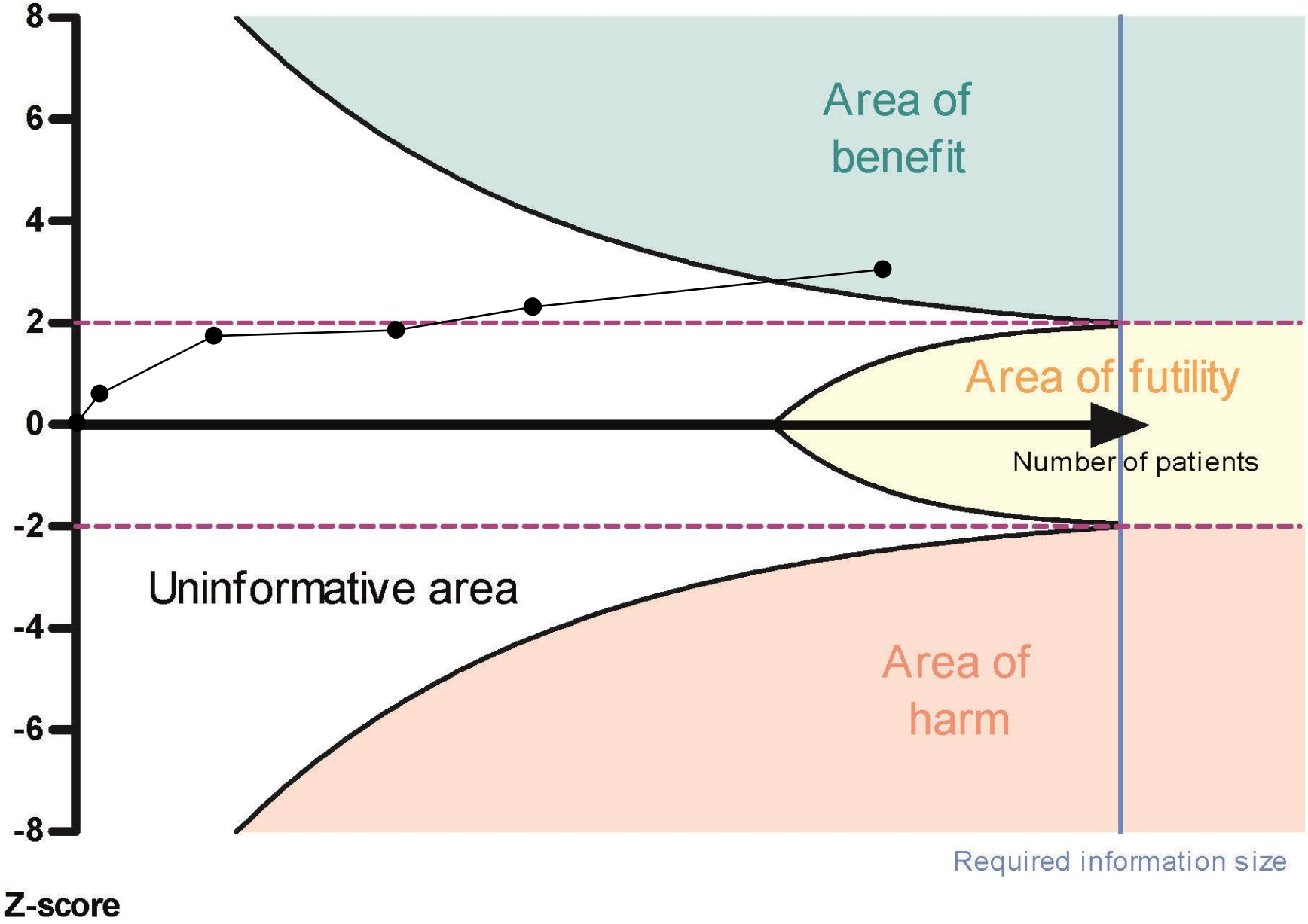
- Interpretation of results…



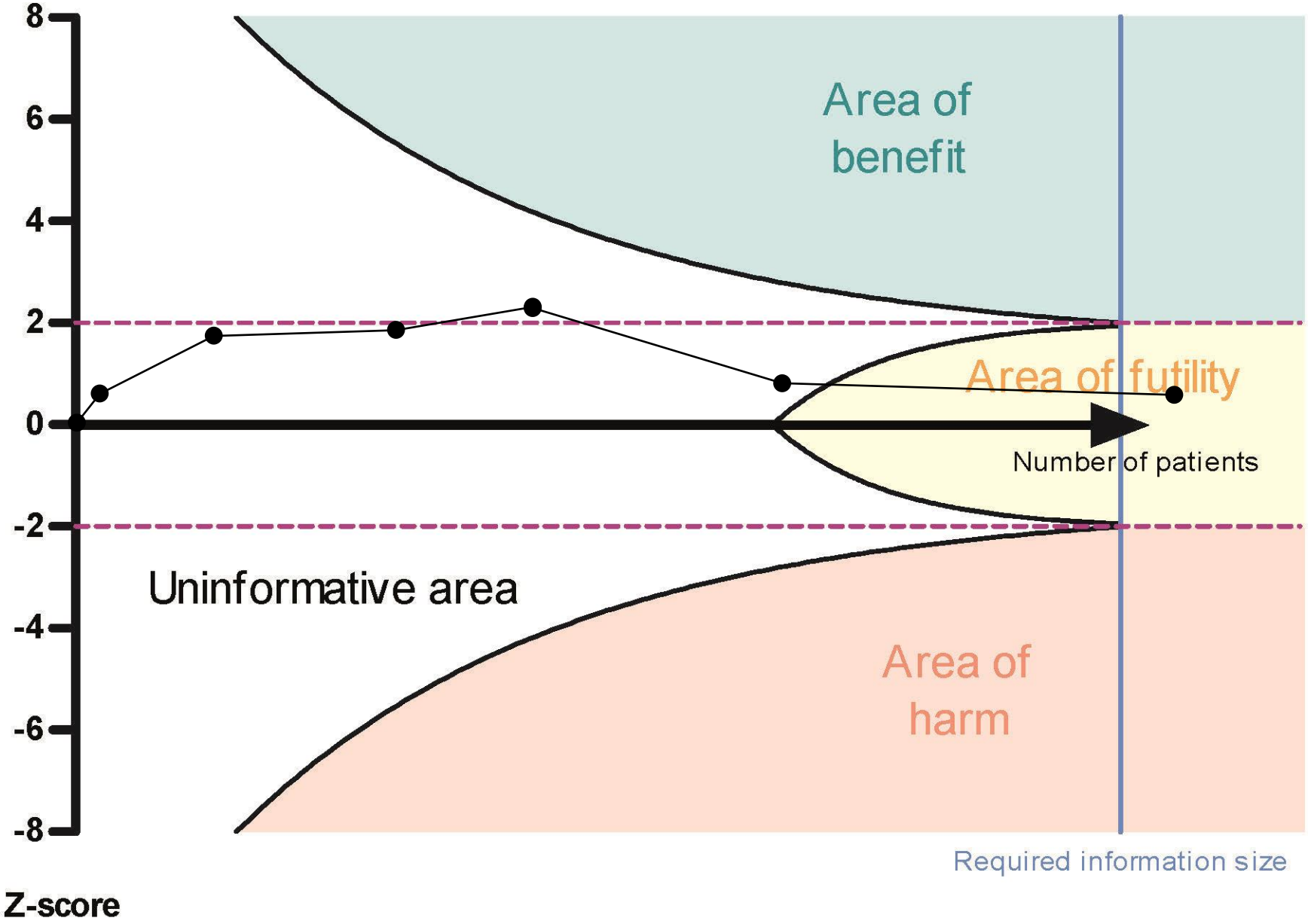


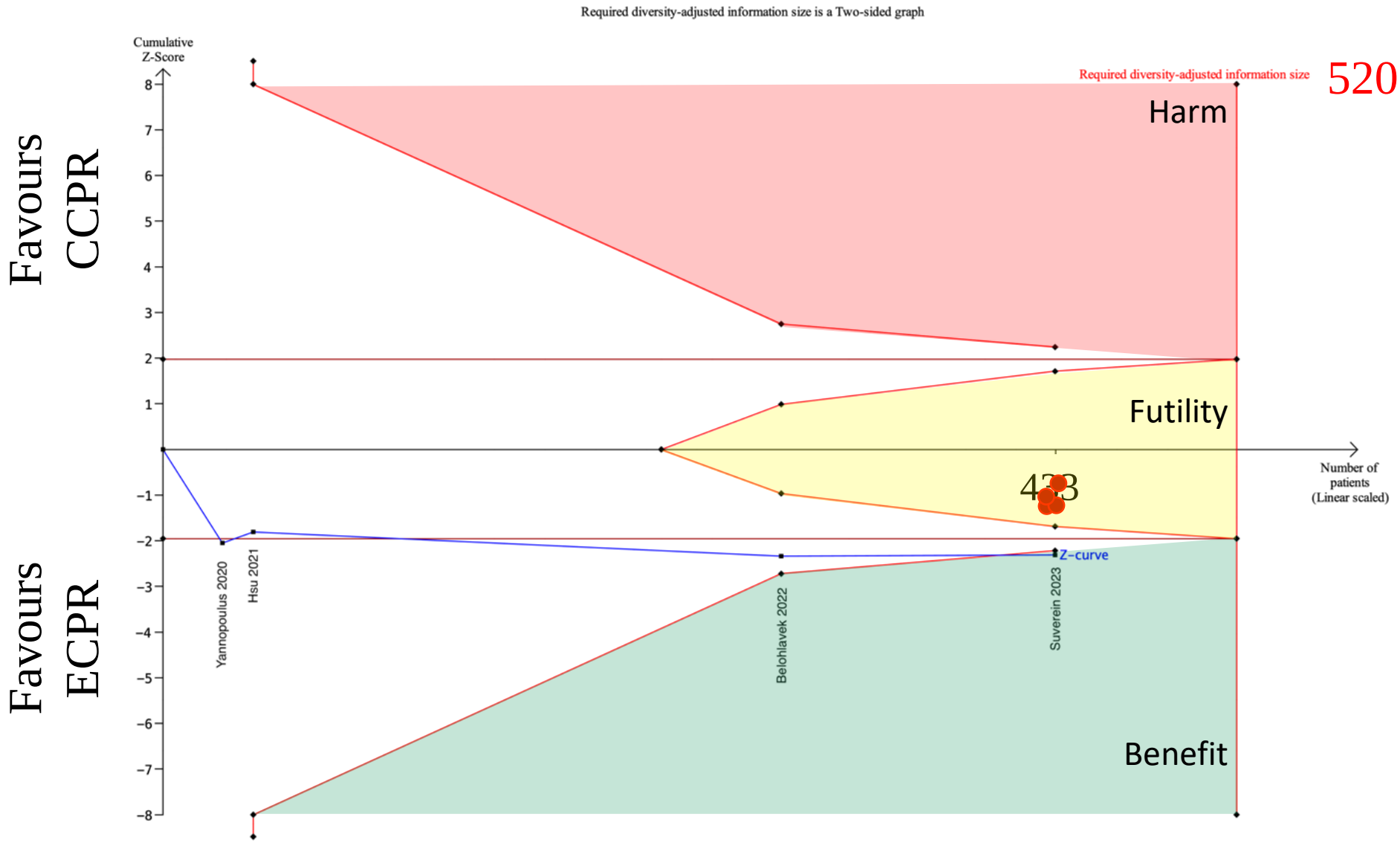
Kiyohara et al. J Cardiovasc Med 2023;24:414-9
Scquizatto et al. Artif Organs. 2023;47:806-16
Ali et al. JACC Cardiovasc Interv. 2023;161825-7
Gomes et al. Intern Emerg Med. 2023;18:2113-20
Huzaifa et al. Pacing Clin Electrophysiol. 2023;46:1246-50

Trial Sequential Analysis



Trial Sequential Analysis





Scquizatto et al. Artif Organs. 2023;47:806-16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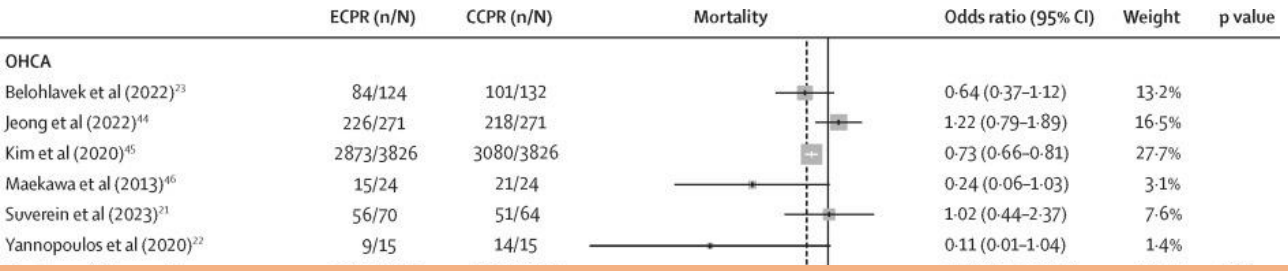
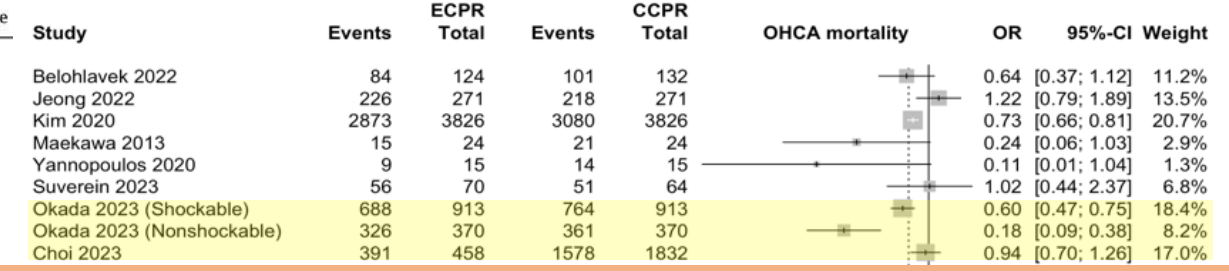
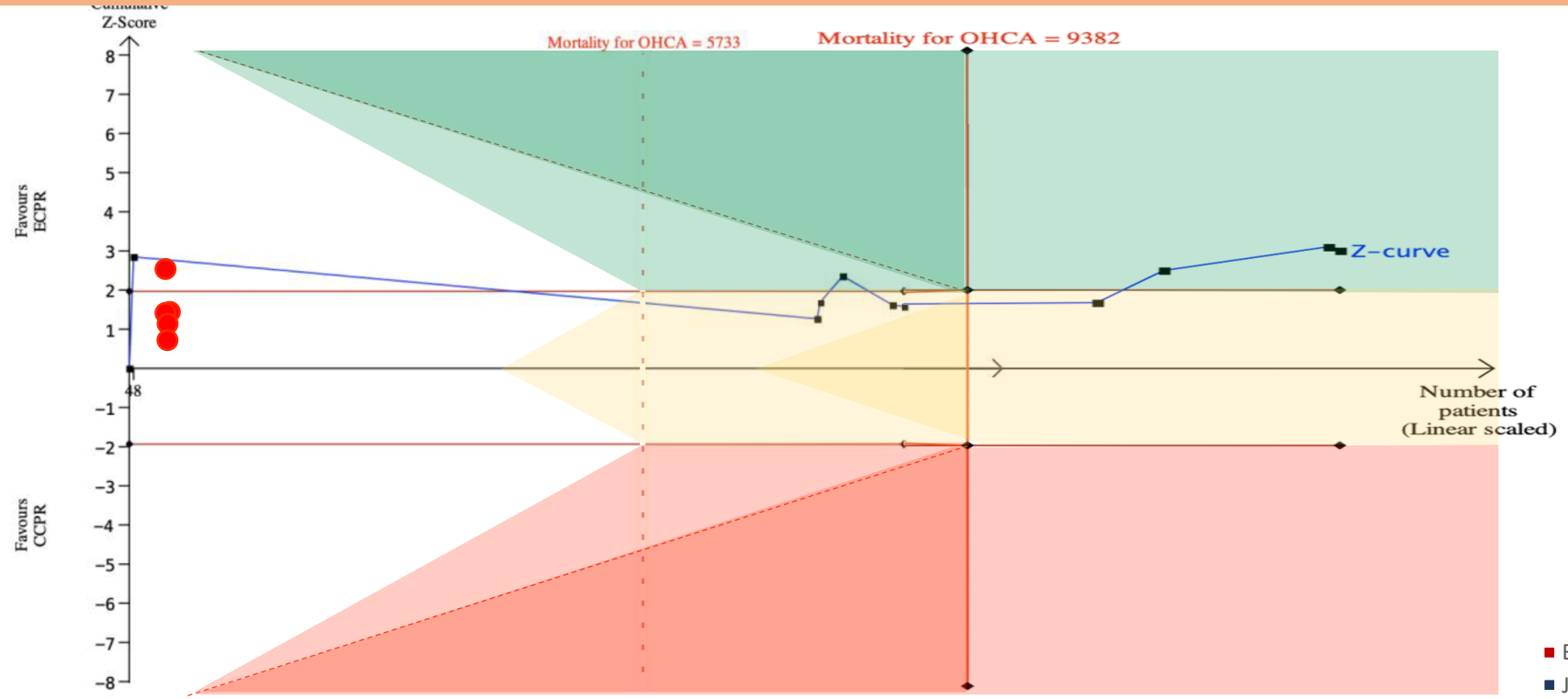
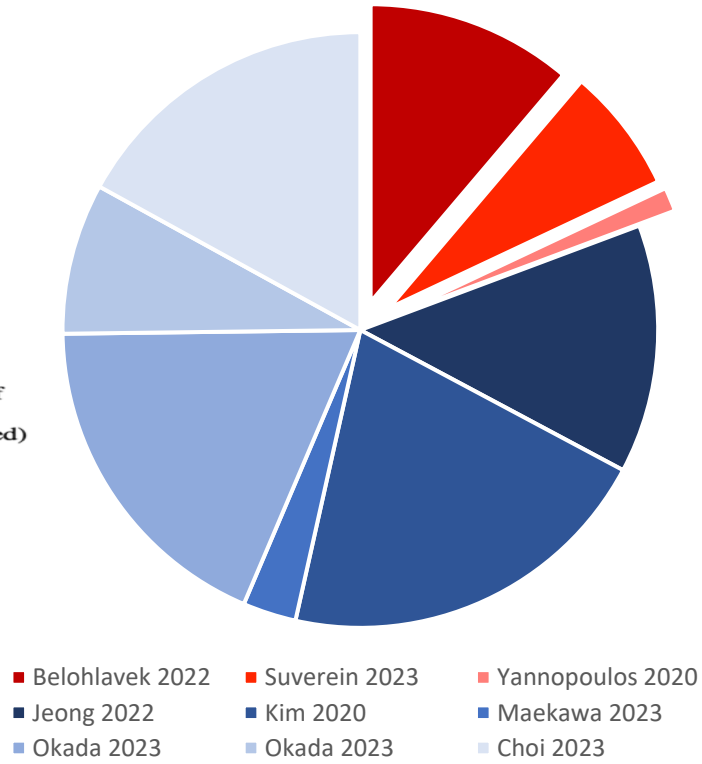




when considering OHCA only, ***no differences were found*** We additionally found a newly ***significant benefit in OHCA***





Low et al. Lancet Respir Med. 2023;11:883-893

Low et al. Crit Care. 2024;28:57


Alpecin
Elegant
ROUBAIX

JAMA | Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome and Posterior Probability of Mortality Benefit in a Post Hoc Bayesian Analysis of a Randomized Clinical Trial

Ewan C. Goligher, MD, PhD; George Tomlinson, PhD; David Hajage, MD, PhD; Duminda N. Wijeysundera, MD, PhD; Eddy Fan, MD, PhD; Peter Jüni, MD; Daniel Brodie, MD; Arthur S. Slutsky, MD; Alain Combes, MD, PhD

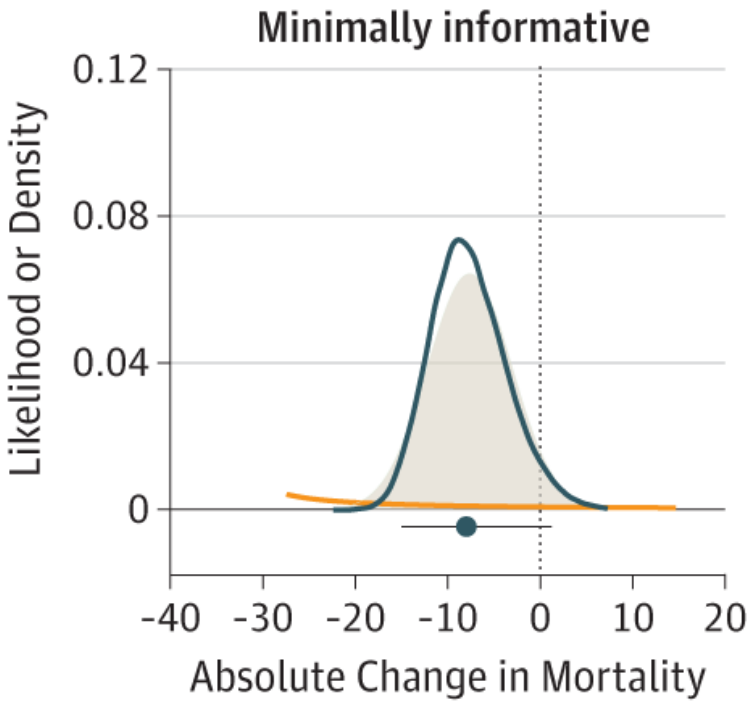


Table 3. Probability That Early ECMO Reduces Mortality by a Proposed Minimum Clinically Important Difference According to Varying Prior Beliefs About Mortality Benefit From ECMO in Patients With Very Severe ARDS

Prior Belief	Posterior Median ARR, % (95% Credible Interval)	Posterior Probability That True ARR Is ≥Specified Threshold, %[a]					
		2%	4%	6%	8%	10%	20%
Reference prior distributions							
Minimally informative	10.6 (−1.8 to 20.0)	92	86	78	67	53	2
Strongly enthusiastic	12.0 (2.1 to 19.9)	98	95	89	79	65	2
Moderately enthusiastic	10.4 (2.0 to 17.2)	97	93	85	71	51	0
Skeptical	7.8 (−3.4 to 16.5)	86	76	62	47	30	0
Strongly skeptical	5.6 (−4.1 to 13.3)	78	63	45	26	13	0
Data-derived prior distribution							
No downweighting of previous studies	13.6 (2.9 to 20.5)	98	96	93	88	79	4
50% Downweighting of previous studies	12.8 (1.9 to 20.4)	97	95	91	83	72	3
75% Downweighting of previous studies	12.1 (1.1 to 20.3)	97	93	88	79	66	3

Abbreviations: ARDS, acute respiratory distress syndrome; ARR, absolute risk reduction; ECMO, extracorporeal membrane oxygenation; EOLIA, ECMO to Rescue Lung Injury in Severe ARDS.

[a] ARR was computed assuming a baseline mortality risk of 46% (based on the mortality rate in the EOLIA control group).

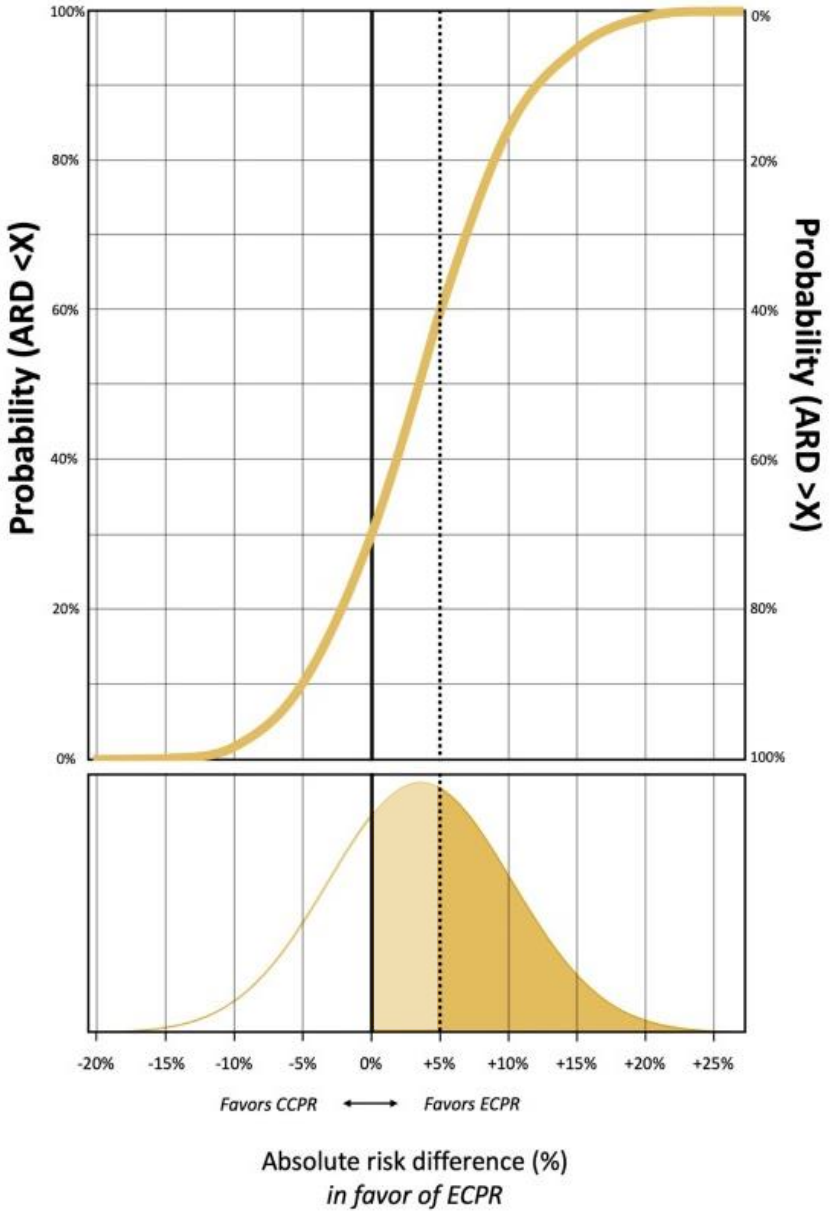
Goligher et al. JAMA 2018;320:2251-9

ESC European Society of Cardiology
European Heart Journal: Acute Cardiovascular Care (2024) **13**, 191–200
https://doi.org/10.1093/ehjacc/zuad130
ORIGINAL SCIENTIFIC PAPER
Emergency Care and Resuscitation

Extracorporeal life support in cardiac arrest: a *post hoc* Bayesian re-analysis of the INCEPTION trial

Samuel Heuts [1,2]*, Anina F. van de Koolwijk[3], Andrea Gabrio[4], Johannes F.H. Ubben[3,5], Iwan C.C. van der Horst[2,3], Thijs S.R. Delnoij[3], Martje M. Suverein[3], Jos G. Maessen[1,2], Roberto Lorusso [1,2†], and Marcel C.G. van de Poll[3,6†]

Outcome	Posterior probabilities: Any benefit (%)	MCID (5% ARD) (%)	Any harm (%)
30 days	70.5	41.7	29.5
6 months	71.6	42.1	28.4



Heuts et al. Eur Heart J Acute Cardiovasc Care 2024;13:191-200

Effect of Intraarrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Invasive Treatment

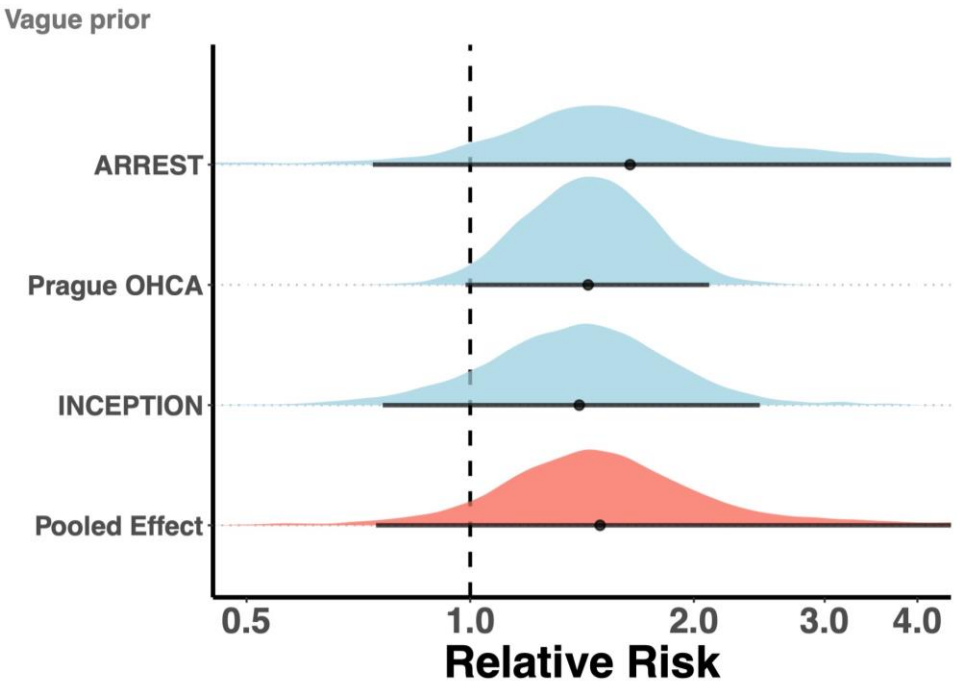
A Post Hoc Bayesian Reanalysis of a Randomized Clinical Trial

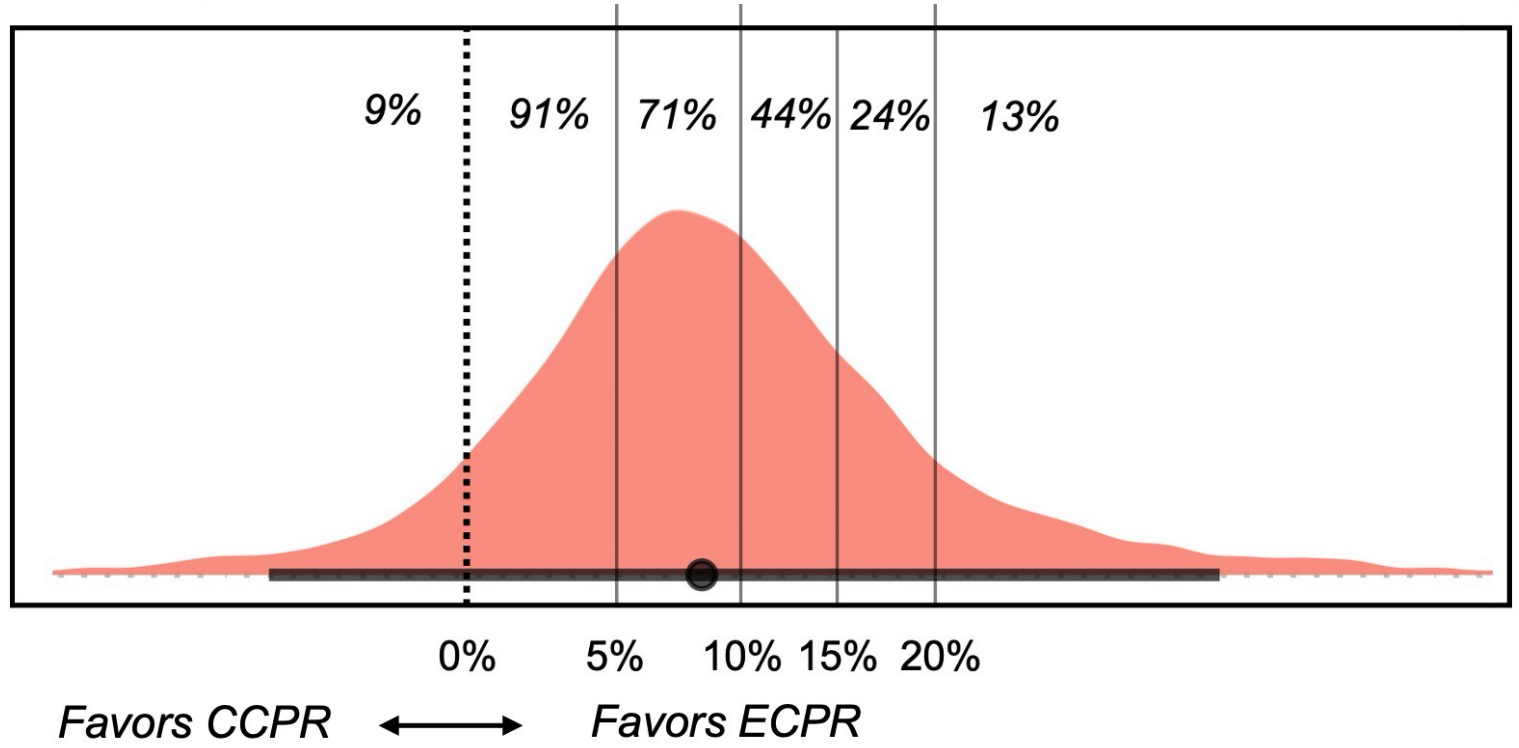
TABLE 1] Bayesian Analysis of the Primary Outcome of Survival With Minimal or No Neurologic Impairment at 180 d

Scenario	Prior OR	Prior SD of log(OR)	OR (95% CI)	Effect Difference, % (95% CI)	Posterior Probability of the Effect Difference > 0, %
Weakly informative	1.00	10.0	1.65 (0.83-2.71)	9.6 (−1.2 to 20.2)	96.1
Mildly enthusiastic	1.70	0.2	1.68 (1.18-2.25)	9.9 (3.8 to 16.2)	99.9
Moderately enthusiastic	2.15	0.5	1.76 (1.01-2.73)	10.8 (1.7 to 20.2)	98.9
Strongly enthusiastic	2.65	1.0	1.70 (0.89-2.76)	10.2 (−0.3 to 20.4)	97.4
Mildly skeptical	1.00	1.0	1.58 (0.84-2.58)	8.9 (−1.7 to 19.0)	95.3
Moderately skeptical	1.00	0.5	1.45 (0.83-2.24)	7.2 (−1.7 to 16.9)	93.6
Strongly skeptical	1.00	0.2	1.18 (0.83-1.58)	3.2 (−3.1 to 9.2)	84.5

Rob et al. Chest 2024;165:368-70

Bayesian meta-analysis of RCT's on ECPR in OHCA





Heuts et al. Manuscript under review

Extracorporeal cardiopulmonary resuscitation for refractory OHCA: lessons from three randomized controlled trials—the trialists' view

Johannes F. H. Ubben[1,2†], Samuel Heuts[3,4†], Thijs S. R. Delnoij[1,5], Martje M. Suverein[1], Anina F. van de Koolwijk[1], Iwan C. C. van der Horst[1,4], Jos G. Maessen[3,4], Jason Bartos[6], Petra Kavalkova[7], Daniel Rob[7], Demetris Yannopoulos[6‡], Jan Bělohlávek[7*‡], Roberto Lorusso[3,4‡], and Marcel C. G. van de Poll[1,8‡]

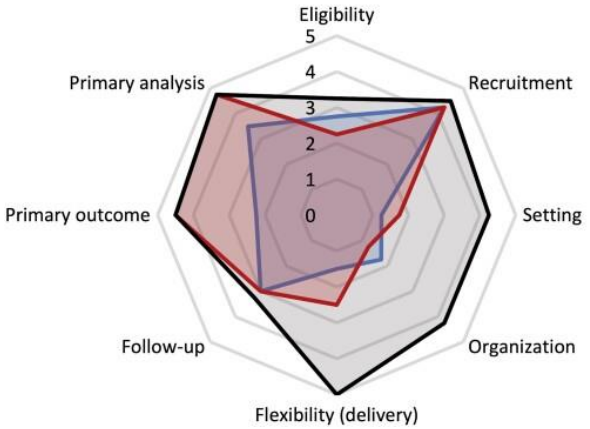

Articles

Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial


JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Intra-arrest Transport, Extracorporeal Cardiopulmonary Resuscitation, and Immediate Invasive Assessment and Treatment on Functional Neurologic Outcome in Refractory Out-of-Hospital Cardiac Arrest
A Randomized Clinical Trial

PRECIS-2 assessment




The NEW ENGLAND JOURNAL of MEDICINE

Early Extracorporeal CPR for Refractory Out-of-Hospital Cardiac Arrest

Explanatory (efficacy) ← Pragmatic (effectiveness) →

Ubben et al. Eur Heart J Acute Cardiovasc Care 2023;24:540-7

Conclusions (general)

- Meta-analyses can provide valuable information on aggregating evidence
- Results and conclusions can be affected by methodological choices
- When information size is limited, Bayesian statistics provide sensible alternative to adding lower quality data
- When evidence is derived from sources with large practice variation it may be better to learn the different lessons from individual trials than to seek a universal treatment effect

Conclusions (ECPR for OHCA)

- RCT's and meta-analyses show that *(there is a high probability that)* ECPR saves lifes

- Clinical effectiveness depends on local infrastructure and expertise – there is no unifying treatment effect

Take away message

"Given the large implications of an ineffective ECPR program, centers should regularly audit their own effectiveness and adjust practice if necessary, not (blindly) point at evidence from explanatory RCT's or meta-analyses"

Merci pour votre attention