

Supplementary Material

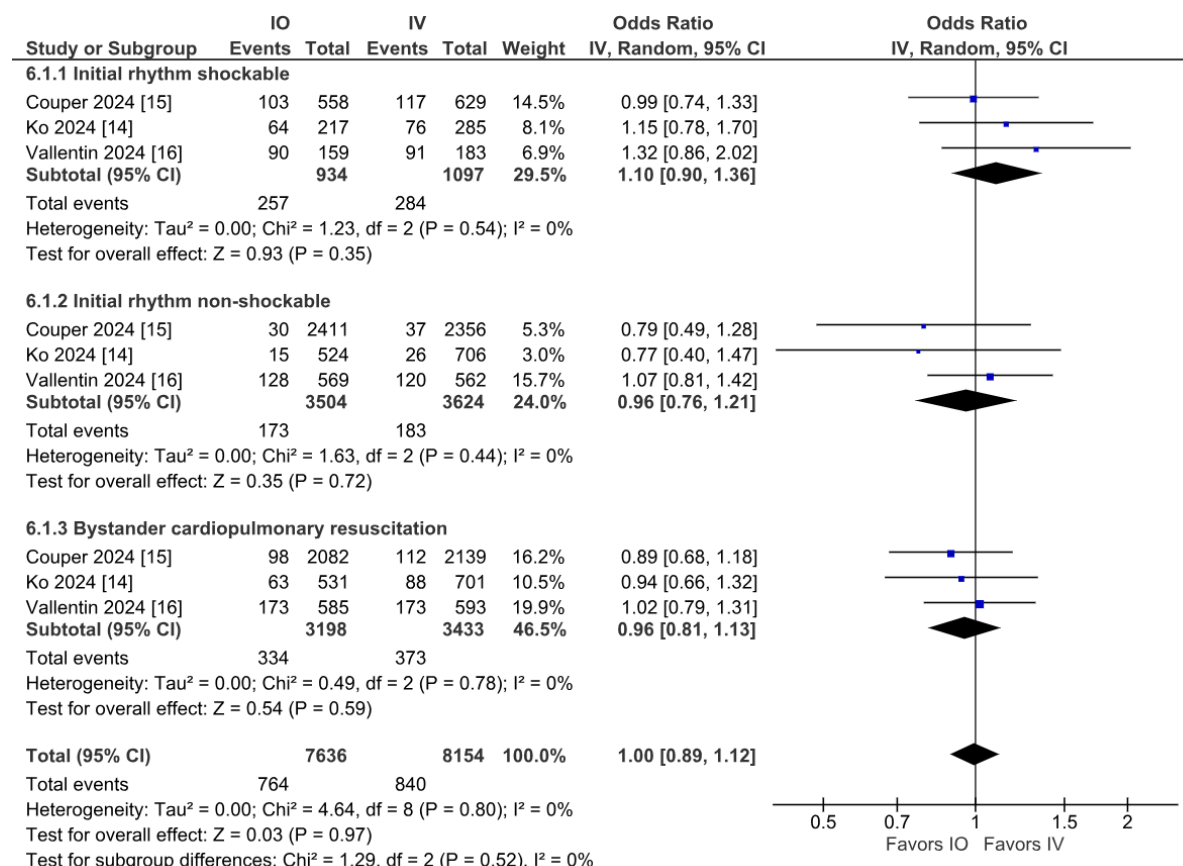
Supplementary Appendix 1

Although subgroup analyses were not pre-specified in the PROSPERO-registered protocol, they were conducted to explore sources of heterogeneity. These analyses assessed survival rates by initial rhythm (shockable vs. non-shockable) and by bystander-performed CPR. Additionally, a leave-one-out meta-analysis was performed for outcomes with high heterogeneity to ensure that no single study disproportionately influenced the pooled estimate.

Supplementary Table 1 Search strategy	
Cochrane	#1 "Drug Route" #2 "Medication Route" #3 "Administration Route" #4 Intraosseous #5 (#1 or #2 or #3 or #4) #6 "Out-of-Hospital" #7 Prehospital #8 "pre-hospital*" #9 "pre hospital*" #10 "ambulance*" #11 "paramedic*" #12 EMS #13 (#6 or #7 or #8 or #9 or #10 or #11 or #12) #14 "cardiac arrest" #15 "heart arrest*" #16 "ventricular fibrillation*" #17 resuscitation #18 (#14 or #15 or #16 or #17) #19 (#5 and #13 and #18)
MEDLINE	#1 "Drug Route" #2 "Medication Route" #3 "Administration Route" #4 Intraosseous #5 (#1 or #2 or #3 or #4) #6 "Out-of-Hospital" #7 Prehospital #8 "pre-hospital*" #9 "pre hospital*" #10 "ambulance*" #11 "paramedic*"

	#12 EMS #13 (#6 or #7 or #8 or #9 or #10 or #11 or #12) #14 "cardiac arrest" #15 "heart arrest*" #16 "ventricular fibrillation*" #17 resuscitation #18 (#14 or #15 or #16 or #17) #19 "randomized controlled trial"[pt] #20 "controlled clinical trial"[pt] #21 randomized[tiab] #22 placebo[tiab] #23 "drug therapy"[sh] #24 randomly[tiab] #25 trial[tiab] #26 groups[tiab] #27 (#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26) #28 (#5 and #13 and #18 and #27)
Embase	#1 "Drug Route" #2 "Medication Route" #3 "Administration Route" #4 Intraosseous #5 (#1 or #2 or #3 or #4) #6 "Out-of-Hospital" #7 Prehospital #8 "pre-hospital*" #9 "pre hospital*" #10 "ambulance*" #11 "paramedic*" #12 EMS #13 (#6 or #7 or #8 or #9 or #10 or #11 or #12) #14 'randomized controlled trial'/exp #15 'controlled clinical trial'/exp #16 randomized:ti,ab #17 placebo:ti,ab #18 'drug therapy':lnk #19 randomly:ti,ab #20 trial:ti,ab #21 groups:ti,ab #22 (#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21) #23 (#5 and #13 and #22)

Supplementary Figure 1. Forest plot for the subgroups analyzed: (6.1.1) Initial shockable rhythm; (6.1.2) Initial non-shockable rhythm; and (6.1.3) Bystander-performed cardiopulmonary resuscitation.



Supplementary Figure 2. Critical appraisal of individual studies according to the Cochrane Collaboration's tool for assessing risk of bias in randomized trials.

		Risk of bias domains					Overall
		D1	D2	D3	D4	D5	
Study	Couper et al., 2024	+	+	+	+	+	+
	Ko et al., 2024	+	+	+	+	+	+
	Vallentin et al., 2024	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
+ Low