Appendix A Review questions according to the PICO Scheme

- Question 1: In adults resuscitated from in-hospital cardiac arrest (P) and treated with TTM (I), survival to hospital discharge (O)
- Question 2: In adults resuscitated from in-hospital cardiac arrest (P) and treated with TTM (I), good neurological outcome, defined as grade 1 or 2 (O) of brain function.

	Hypothe	rmia	No hypoth	ermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.3.1 1							
Kory, P 2012	5	16	5	17	2.5%	1.09 [0.25, 4.82]	
Paul,S,Chan 2016	170	412	389	882	97.5%	0.89 [0.70, 1.13]	
Subtotal (95% CI)		428		899	100.0 %	0.89 [0.71, 1.13]	\bullet
Total events	175		394				
Heterogeneity: Tau ² =	= 0.00; Chi ^a	= 0.07	df = 1 (P = 1	0.79); l² =	= 0%		
Test for overall effect	Z = 0.93 (F	P = 0.35	i)				
Total (95% CI)		428		899	100.0%	0.89 [0.71, 1.13]	•
Total events	175		394				
Heterogeneity: Tau ² =	= 0.00; Chi ⁼	= 0.07	df = 1 (P = 1	0.79); l² =	= 0%		
Test for overall effect:	Z = 0.93 (F	P = 0.35	5)				0.01 0.1 1 10 10
Test for subaroup dif	ferences: N	lot app	licable				Favours [No hypothermia] Favours [Hypothermia]

Figure S1 Survival to hospital discharge in shockable initial rhythms.

Hypothermia No hypothermia Odds Ratio Odds Ratio Total Events Total Weight M-H, Random, 95% Cl M-H, Random, 95% Cl Study or Subgroup Events 1.4.1 small samples Chieh-Jen Wang, 2020 0.10 [0.04, 0.25] 23 35 216 227 13.9% Kory, P 2012 5 17 5 16 8.1% 0.92 [0.21, 4.05] Perman, S. M. 2015 42 21 120 15.4% 1.89 [0.83, 4.27] 12 Wang, C. H. 2016 9 22 135 656 14.6% 2.67 [1.12, 6.38] Subtotal (95% CI) 116 1019 52.0% 0.82 [0.17, 3.99] Total events 19 377 Heterogeneity: Tau² = 2.32; Chi² = 31.36, df = 3 (P < 0.00001); l² = 90% Test for overall effect: Z = 0.24 (P = 0.81) 1.4.2 large samples Nichol, G. 2013 58 214 2454 8102 23.2% 0.86 [0.63, 1.16] Paul,S,Chan 2016 417 1524 1084 3714 24.8% 0.91 [0.80, 1.04] Subtotal (95% CI) 1738 11816 48.0% 0.90 [0.80, 1.02] 3538 Total events 475 Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); l² = 0% Test for overall effect: Z = 1.62 (P = 0.11) 0.86 [0.52, 1.44] Total (95% CI) 1854 12835 100.0% Total events 524 3915 Heterogeneity: Tau² = 0.27; Chi² = 31.48, df = 5 (P < 0.00001); l² = 84% 0.01 0.1 10 100 Test for overall effect: Z = 0.56 (P = 0.57) Favours [No hypothermia] Favours [Hypothermia] Test for subaroup differences: $Chi^2 = 0.01$. df = 1 (P = 0.91). $I^2 = 0\%$

Figure S2 Survival to hospital discharge in different sample content.

	Hypothe	rmia	No hypoth	iermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.5.1 small samples							
Chieh-Jen Wang, 2020	1	26	57	154	7.4%	0.07 [0.01, 0.52]	·
Kory, P 2012	4	17	5	16	10.6%	0.68 [0.15, 3.16]	
Perman, S. M. 2015	9	42	16	120	17.3%	1.77 [0.72, 4.39]	
Wang, C. H. 2016	7	22	53	656	16.9%	5.31 [2.07, 13.59]	_
Subtotal (95% CI)		107		946	52.1%	0.97 [0.19, 5.03]	
Total events	21		131				
Heterogeneity: Tau ² = 2.3	3; Chi ⁼ = 2	21.10, di	f = 3 (P = 0.)	0001); i ^z :	= 86%		
Test for overall effect: Z =	0.04 (P=	0.97)					
1.5.2 large samples							
Nichol, G. 2013	17	91	1591	8102	22.2%	0.94 [0.55, 1.60]	
Paul,S,Chan 2016	246	1443	725	3529	25.7%	0.79 [0.68, 0.93]	-
Subtotal (95% CI)		1534		11631	47.9%	0.81 [0.69, 0.94]	\blacklozenge
Total events	263		2316				
Heterogeneity: Tau ² = 0.0	10; Chi ² = 0).35, df=	= 1 (P = 0.5	5); I ² = 09	6		
Test for overall effect: Z =	2.76 (P=	0.006)					
Total (95% CI)		1641		12577	100.0%	1.07 [0.56, 2.05]	+
Total events	284		2447				
Heterogeneity: Tau ² = 0.4	2; Chi ² = 2	4.25, di	f = 5 (P = 0.1	0002); I ² :	= 79%		
Test for overall effect: Z =	•						0.01 0.1 1 10 100
Test for subaroup differe	nces: Chi²	= 0.05.	df = 1 (P = 1	0.83). I r =	0%		Favours [No hypothermia] Favours [Hypothermia]

Figure S3 Good neurological outcomes in different sample content.

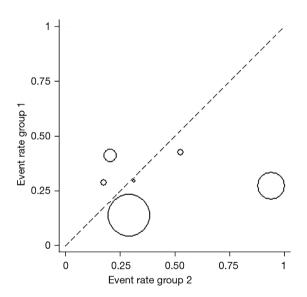


Figure S4 Survival to hospital discharge L'Abbe plot.

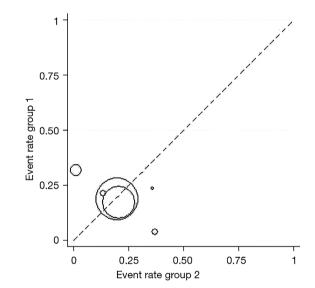


Figure S5 Good neurological outcomes L'Abbe plot.

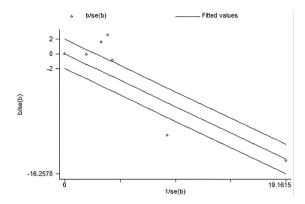


Figure S6 Survival to hospital discharge Galbraith plot.

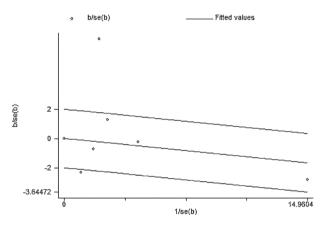


Figure S7 Good neurological outcomes Galbraith plot.

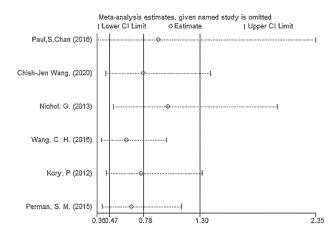


Figure S8 Impact map of a single study in the discharged survival group.

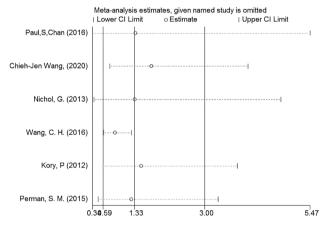


Figure S9 Impact map of a single study in the good neurological outcome group.

	Hypothe	rmia	NO hypoth	nermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chieh-Jen Wang, 2020	11	26	81	154	2.3%	0.66 [0.29, 1.53]	
Kory, P 2012	5	17	5	16	0.6%	0.92 [0.21, 4.05]	
Nichol, G. 2013	58	214	2454	8102	15.9%	0.86 [0.63, 1.16]	
Paul,S,Chan 2016	417	1524	1084	3714	79.0%	0.91 [0.80, 1.04]	
Perman, S. M. 2015	12	42	21	120	1.3%	1.89 [0.83, 4.27]	+
Wang, C. H. 2016	9	22	135	656	0.9%	2.67 [1.12, 6.38]	
Total (95% CI)		1845		12762	100.0%	0.93 [0.82 , 1.0 4]	•
Total events	512		3780				
Heterogeneity: Chi ² = 9.5	50, df = 5 (P	= 0.09)	; l² = 47%				
Test for overall effect: Z =	= 1.25 (P = 1	0.21)					0.01 0.1 1 10 100 Favours [NO hypothermia] Favours [Hypothermia]

Figure S10 Randomized effect model diagram of the discharged survival group.

	Hypothe	rmia	NO hypoth	nermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chieh-Jen Wang, 2020	1	26	57	154	3.9%	0.07 [0.01, 0.52]	·
Kory, P 2012	4	17	5	16	1.0%	0.68 [0.15, 3.16]	
Nichol, G. 2013	17	91	1591	8102	7.1%	0.94 [0.55, 1.60]	
Paul,S,Chan 2016	246	1443	725	3529	85.9%	0.79 [0.68, 0.93]	
Perman, S. M. 2015	9	42	16	120	1.6%	1.77 [0.72, 4.39]	
Wang, C. H. 2016	7	22	53	626	0.6%	5.05 [1.97, 12.92]	
Total (95% Cl)		1641		12547	100.0%	0.82 [0.71, 0.95]	◆
Total events	284		2447				
Heterogeneity: Chi ² = 23.	44, df = 5 ((P = 0.0	003); l² = 79	%			
Test for overall effect: Z =	2.70 (P =	0.007)					0.01 0.1 1 10 100 Favours [NO hypothermia] Favours [Hypothermia]

Figure S11 Neurological function randomization effect model diagram.

	Hypothe	rmia	NO hypoth	iermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Chieh-Jen Wang, 2020	11	26	81	154	2.0%	0.66 [0.29, 1.53]	
Kory, P 2012	5	17	5	16	0.6%	0.92 [0.21, 4.05]	
Nichol, G. 2013	58	214	2454	8102	15.2%	0.86 [0.63, 1.16]	
Paul,S,Chan 2016	417	1524	1084	3714	80.0%	0.91 [0.80, 1.04]	
Perman, S. M. 2015	12	42	21	120	2.1%	1.89 [0.83, 4.27]	+
Wang, C. H. 2016	9	22	135	656	0.0%	2.67 [1.12, 6.38]	
Total (95% Cl)		1823		12106	100.0%	0.91 [0.81, 1.03]	•
Total events	503		3645				
Heterogeneity: Tau ² = 0.0	00; Chi ² = 3	.76, df=	= 4 (P = 0.44	l); I² = 0%			
Test for overall effect: Z =	•						0.01 0.1 1 10 100 Favours [NO hypothermia] Favours [Hypothermia]

Figure S12 Single study removal impact diagram of discharge survival.

	Hypothe	rmia	NO hypoth	ermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Chieh-Jen Wang, 2020	1	26	57	154	4.9%	0.07 [0.01, 0.52]	← → → → →
Kory, P 2012	4	17	5	16	7.9%	0.68 [0.15, 3.16]	
Nichol, G. 2013	17	91	1591	8102	28.4%	0.94 [0.55, 1.60]	
Paul,S,Chan 2016	246	1443	725	3529	41.8%	0.79 [0.68, 0.93]	
Perman, S. M. 2015	9	42	16	120	17.0%	1.77 [0.72, 4.39]	-
Wang, C. H. 2016	7	22	53	626	0.0%	5.05 [1.97, 12.92]	
Total (95% Cl)		1619		11921	100.0%	0.84 [0.52, 1.35]	-
Total events	277		2394				
Heterogeneity: Tau ² = 0.1	13; Chi ² = 9	1.13, df=	= 4 (P = 0.08	i); I² = 56	%		
Test for overall effect: Z =	: 0.74 (P =	0.46)					0.01 0.1 1 10 100 Favours [NO hypothermia] Favours [Hypothermia]

Figure S13 Single study removal impact diagram of neurological outcome.

	Hypothe	rmia	No hypoth	nermia		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.4.1 small samples							
Chieh-Jen Wang, 2020	23	35	216	227	13.9%	0.10 [0.04, 0.25]	
Kory, P 2012	5	17	5	16	8.1%	0.92 [0.21, 4.05]	
Perman, S. M. 2015	12	42	21	120	15.4%	1.89 [0.83, 4.27]	
Wang, C. H. 2016	9	22	135	656	14.6%	2.67 [1.12, 6.38]	
Subtotal (95% CI)		116		1019	52.0 %	0.82 [0.17, 3.99]	
Total events	49		377				
Heterogeneity: Tau ² = 2.3	2; Chi ² = 3	1.36, df	f= 3 (P < 0.1	00001); P	°= 90%		
Test for overall effect: Z =	0.24 (P =)	D.81)					
1.4.2 large samples							
Nichol, G. 2013	58	214	2454	8102	23.2%	0.86 [0.63, 1.16]	-=-
Paul,S,Chan 2016	417	1524	1084	3714	24.8%	0.91 [0.80, 1.04]	=
Subtotal (95% CI)		1738		11816	48.0 %	0.90 [0.80, 1.02]	•
Total events	475		3538				
Heterogeneity: Tau ² = 0.0	10; Chi² = 0	.15, df=	= 1 (P = 0.7	0); i² = 0%	6		
Test for overall effect: Z =	1.62 (P = 1	D.11)					
Total (95% CI)		1854		12835	100.0%	0.86 [0.52, 1.44]	-
Total events	524		3915				
Heterogeneity: Tau ² = 0.2	7; Chi ² = 3	1.48, df	f= 5 (P < 0.1	00001); P	²= 84%		
Test for overall effect: Z =							
Test for subaroup differen	nces: Chi²	= 0.01.	df=1 (P=)	0.91). I ^z =	0%		Favours [No hypothermia] Favours [Hypothermia]

Figure S14 Funnel chart.