

Table e-1. Evidence tables for “Reducing brain injury following cardiopulmonary resuscitation”

Author, y	Classes	Population	Definition of coma	Intervention	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
VT/VF TH vs NT																	
Hypothermia after Cardiac Arrest Study Group, 2002 ^{e6}	I	OHCA, cardiac origin	Comatose (no response to verbal commands after ROSC)	TH (32°C-34°C)	NT	CPC 1-2 at 6 mo	VT/VF	No details provided	273	54	137	39%	75	136	55%	16%	4%-27%
Hypothermia after Cardiac Arrest Study Group, 2002 ^{e6}	I	OHCA, cardiac origin	Comatose (no response to verbal commands after ROSC)	TH (32°C-34°C)	NT	Mortality at 6 mo	VT/VF	No details provided	275	76	138	55%	56	137	41%	-14%	-26% to -3%
Bernard, 2002 ^{e8}	I	OHCA, cardiac origin	Persistent coma after ROSC” coma not defined	TH (32°C-34°C)	NT	Good outcome at discharge	VT/VF	“active life support was withdrawn from most patients who remained deeply comatose at 72 hours”	77	9	34	26%	21	43	49%	22%	1%-43%
Nielsen, 2013 ^{e9}	I	OHCA, cardiac origin	Unconscious GCS ≤ 8	TTM (36°C)	TH (34°C)	CPC 1-2 at 180 d	Combined	Recommendation made by blinded physician at 72 h after warming for comatose survivors. Protocol for withdrawal of life support	939	222	473	47%	224	466	48%	1%	-5% to 8%
Nielsen, 2013 ^{e9}	I	OHCA, cardiac origin	Unconscious GCS ≤ 8	TTM (36°C)	TH (34°C)	Survival at end of trial	Combined	Recommendation made by blinded physician at 72 h after warming for comatose survivors. Protocol for	939	238	473	50%	241	466	52%	1%	-5% to 8%

Author, y	Classes	Population	Definition of coma	Intervention	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
								withdrawal of life support									
Nielsen, 2013 ^{e9}	I	OHCA, cardiac origin	Unconscious GCS ≤ 8	TTM (36°C)	TH (34°C)	Survival at end of trial	VT/VF	Recommendation made by blinded physician at 72 h after warming for comatose survivors. Protocol for withdrawal of life support	752	222	375	59%	227	377	60%	1%	-6% to 8%
Lopez-de-Sa, 2012 ^{e10}	I	OHCA, cardiac origin	GCS after ROSC 8 or less	TH (32°C)	TH (34°C)	Survival free from severe dependence at 6 mo	VT/VF	"Patients who remained deeply comatose after 5 days of evolution, limitation of active life support was decided in agreement with their representatives"	26	2	13	15%	8	13	62%	46%	13%-79%
Lopez-de-Sa, 2012 ^{e10}	I	OHCA, cardiac origin	GCS after ROSC 8 or less	TH (32°C)	TH (34°C)	Survival at 6 mo	VT/VF	"Patients who remained deeply comatose after 5 days of evolution, limitation of active life support was decided in agreement with their	26	2	13	15%	8	13	62%	46%	13%-79%

Author, y	Clas s	Population	Definition of coma	Intervention s	Control	Outcome	Group	WOLST	Total patient s	Outcom e control	Total contr ol	Risk contr ol	Outcome treatme nt	Total treatme nt	Risk treatme nt	Risk differenc e	95% CI
								representatives "									
PEA/Asystole: TH vs NT																	
Testori 2011 ^{e17}	III	OHCA, nontraumat ic	GCS 8 or less	TH (32°C- 34°C)	NT	Good neurologic outcome at 6 mo	PEA/asys	Not provided	374	55	239	23%	47	135	35%	12%	2%- 21%
Testori 2011 ^{e17}	III	OHCA, nontraumat ic	GCS 8 or less	TH (32°C- 34°C)	NT	Death at 6 mo	PEA/asys	Not provided	374	180	239	75%	82	135	61%	-15%	-24% to - 5%
Testori 2011 ^{e17}	III	OHCA, nontraumat ic	GCS 8 or less	TH (32°C- 34°C)	NT	Survival at 6 mo	PEA/asys	Not provided	374	59	239	25%	53	135	39%	15%	5%- 24%
Testori 2011 ^{e17}	III	OHCA, nontraumat ic	GCS 8 or less	TH (32°C- 34°C)	NT	Survival at 6 mo	PEA/asys	Not provided	374	59	239	25%	53	135	39%	15%	5%- 24%
Lundbye, 2012 ^{e18}	III	OHCA and IHCA	GCS 8 or less	TH (32°C- 34°C)	NT	CPC 1-2 at discharge	PEA/asys	How the decision was made was not provided. Similar proportion of WOLST in both groups	100	6	48	13%	15	52	29%	16%	1%- 32%
Lundbye, 2012 ^{e18}	III	OHCA and IHCA	GCS 8 or less	TH (32°C- 34°C)	NT	Survival at discharge	PEA/asys	How the decision was made was not provided. Similar proportion of WOLST in both groups	100	9	48	19%	20	52	38%	20%	3%- 37%
Arrich, 2007 ^{e11}	III	OHCA and IHCA, nontraumat ic	Not responding to verbal commands	TH (32°C- 34°C)	NT	Mortality at discharge	PEA/asys	Not specified	197	59	73	81%	79	124	64%	-17%	-29% to - 5%
Arrich, 2007 ^{e11}	III	OHCA and IHCA,	Not responding to	TH (32°C- 34°C)	NT	Survival at discharge	PEA/asys	Not specified	197	14	73	19%	45	124	36%	17%	5%- 29%

Author, y	Class	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
		nontraumatic	verbal commands														
Arrich, 2007 ^{e11}	III	OHCA and IHCA, nontraumatic	Not responding to verbal commands	TH (32°C-34°C)	NT	CPC 3-5 at discharge	PEA/asys	Not specified	197	59	73	81%	89	124	72%	-9%	-21% to 3%
Arrich, 2007 ^{e11}	III	OHCA and IHCA, nontraumatic	Not responding to verbal commands	TH (32°C-34°C)	NT	CPC 1-2 at discharge	PEA/asys	Not specified	197	14	73	19%	35	124	28%	9%	-3% to 21%
Pfeifer, 2011 ^{e12}	III	OHCA and IHCA, nontraumatic	Unresponsive one hour after ROSC	TH (32°C-34°C)	NT	Mortality at 1 mo	PEA/asys	Not specified	110	22	39	56%	50	71	70%	14%	-5% to 33%
Pfeifer, 2011 ^{e12}	III	OHCA and IHCA, nontraumatic	Unresponsive one hour after ROSC	TH (32°C-34°C)	NT	Survival at 1 mo	PEA/asys	Not specified	110	17	39	44%	21	71	30%	-14%	-33% to 5%
Storm, 2012 ^{e19}	III	OHCA and IHCA	Based on current guidelines	TH (33°C)	NT	CPC 1-2 at ICU discharge	PEA/asys	Not specified	175	16	88	18%	24	87	28%	9%	-3% to 22%
Dumas 2011 ^{e13}	III	OHCA, nontraumatic	Not defined	TH (32°C-34°C)	NT	CPC 1-2 at discharge	PEA/asys	Not specified	437	30	176	17%	38	261	15%	-2%	-9% to 5%
Don 2009 ^{e14}	III	OHCA, nontraumatic	Unconscious after ROSC	TH (32°C-34°C)	NT	Survival at discharge	PEA/asys	Not specified	313	37	191	19%	26	122	21%	2%	-7% to 11%
Don 2009 ^{e14}	III	OHCA, nontraumatic	Unconscious after ROSC	TH (32°C-34°C)	NT	Good neuro status at discharge	PEA/asys	Not specified	313	17	191	9%	14	122	11%	3%	-4% to 10%
Vaahersalo, 2013 ^{e15}	III	OHCA, any cause	"unconscious at hospital or ICU admission"	TH (32°C-34°C)	NT	CPC 1-2 at 1 y	VT/VF	Not specified	281	9	40	23%	138	241	57%	35%	20%-49%
Vaahersalo, 2013 ^{e15}	III	OHCA, any cause	"unconscious at hospital or ICU admission"	TH (32°C-34°C)	NT	Survival at 1 y	VT/VF	Not specified	281	11	40	28%	149	241	62%	34%	19%-49%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Vaahersalo, 2013 ^{e15}	III	OHCA, any cause	"unconscious at hospital or ICU admission"	TH (32°C-34°C)	NT	CPC 1-2 at 1 y	PEA/asys	Not specified	223	24	153	16%	13	70	19%	3%	-8% to 14%
Vaahersalo, 2013 ^{e15}	III	OHCA, any cause	"unconscious at hospital or ICU admission"	TH (32°C-34°C)	NT	Survival at 1 y	PEA/asys	Not specified	223	29	153	19%	19	70	27%	8%	-4% to 20%
Vaahersalo, 2013 ^{e15}	III	OHCA, any cause	"unconscious at hospital or ICU admission"	TH (32°C-34°C)	NT	Survival at hospital discharge	PEA/asys	Not specified	223	48	153	31%	26	70	37%	6%	-8% to 19%
Sung, 2016 ^{e20}	III	OHCA, non-traumatic	N/A; excluded "patients awake and alert in the emergency department"	TH (32°C-34°C)	NT	CPC-12 at discharge	PEA/asys	Not specified	1423	41	827	5%	83	596	14%	8%	5-12%
Sung, 2016 ^{e20}	III	OHCA, non-traumatic	N/A; excluded "patients awake and alert in the emergency department"	TH (32°C-34°C)	NT	CPC-12 at discharge	PEA/asys	Not specified	1423	132	827	16%	180	596	30%	14%	10-19%
Hachimi-Idrissi 2001 ^{e22}	III	OHCA, presumed cardiac origin	Unresponsive after OHCA, GCS<7	Helmet device to achieve 34°C	NT	Survival to discharge	PEA/asys	Not specified	30	1	14	7%	3	16	19%	12%	-16% to 37%
Kory, 2012 ^{e21}	III	IHCA	Unresponsive after IHCA	TH (32°C-34°C)	NT	CPC 1-2 at discharge	Mixed	Not specified	33	5	16	31%	4	17	24%	-8%	-38% to 23%
Kory, 2012 ^{e21}	III	IHCA	Unresponsive after IHCA	TH (32°C-34°C)	NT	Survival to discharge	Mixed	Not specified	33	5	16	31%	5	17	29%	-2%	-33% to 30%
Kory, 2012 ^{e21}	III	IHCA	Unresponsive after IHCA	TH (32°C-34°C)	NT	CPC 1-2 at discharge	PEA/asys	Not specified	20	4	9	44%	3	11	27%	-17%	-59% to 25%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Nichol, 2013 ^{e16}	III	IHCA, general ward, nontraumatic	Patients who received induced hypothermia; precise definition for coma not provided	TH (32°C-34°C)	NT	CPC 1-2 at discharge	Combined	Not specified	8,316	1,591	8,102	20%	40	214	19%	-1%	-6% to 4%
Prehospital cooling																	
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	Mortality at discharge	VF	Not specified	583	103	291	35%	109	292	37%	2%	-6% to 10%
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	Survival at discharge	VF	Not specified	583	188	291	65%	183	292	63%	-2%	-10% to 6%
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	Mortality at discharge	PEA/asys	Not specified	776	318	380	84%	320	396	81%	-3%	-8% to 2%
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	Survival at discharge	PEA/asys	Not specified	776	62	380	16%	76	396	19%	3%	-2% to 8%
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	CPC 1-2 at discharge	VF	Not specified	583	180	291	62%	168	292	58%	-4%	-12% to 4%
Kim, 2014 ^{e34}	I	OHCA, any cause	Unresponsive	Prehospital cooling	No prehospital cooling	CPC 1-2 at discharge	PEA/asys	Not specified	776	51	380	13%	57	396	14%	1%	-4% to 6%
Castrén, 20110 ^{e35}	I	OHCA, any cause	Pulseless at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Survival at discharge	VF	Not specified	37	10	21	48%	10	16	63%	15%	-17% to 47%
Castrén, 20110 ^{e35}	I	OHCA, any cause	Pulseless at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Survival at discharge	PEA/asys	Not specified	37	3	21	14%	4	16	25%	11%	-15% to 37%
Castrén, 20110 ^{e35}	I	OHCA, any cause	Pulseless at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	CPC 1-2 at discharge	VF	Not specified	37	6	21	29%	8	16	50%	21%	-10% to 53%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Castrén, 2011 ^{e35}	I	OHCA, any cause	Pulseless at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	CPC 1-2 at discharge	PEA/asys	Not specified	37	3	21	14%	3	16	19%	4%	-20% to 29%
Bernard, 2010 ^{e36}	I	OHCA	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Favorable outcome at discharge (discharge to home or rehab)	VF	Not specified	234	61	116	53%	56	118	47%	-5%	-18% to 8%
Bernard, 2010 ^{e36}	I	OHCA	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Mortality at discharge	VF	Not specified	234	54	116	47%	62	118	53%	6%	-7% to 19%
Bernard, 2010 ^{e36}	I	OHCA	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Survival at discharge	VF	Not specified	234	62	116	53%	56	118	47%	-6%	-19% to 7%
Bernard, 2010 ^{e36}	I	OHCA, any cause	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Favorable outcome at discharge (discharge to home or rehab)	PEA/asys	Not specified	163	7	81	9%	10	82	12%	4%	-6% to 13%
Bernard, 2010 ^{e36}	I	OHCA, any cause	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Mortality at discharge	PEA/asys	Not specified	163	74	81	91%	71	82	87%	-5%	-14% to -5%
Bernard, 2010 ^{e36}	I	OHCA, any cause	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Survival at discharge	PEA/asys	Not specified	163	7	81	9%	11	82	13%	5%	-5% to 14%
Bernard, 2010 ^{e36}	I	OHCA, cardiac origin	ROSC at randomization, otherwise not defined	Prehospital cooling	No prehospital cooling	Favorable outcome at discharge (discharge to home or rehab)	Cardiac cause	Not specified	90	3	43	7%	8	47	17%	10%	-3% to 23%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Kim, 2007 ^{e40}	I	OHCA, nontraumatic	Unresponsive	Prehospital cooling	No prehospital cooling	Survival at discharge	VF	Not specified	51	10	22	45%	19	29	66%	20%	-7% to 47%
Kim, 2007 ^{e40}	I	OHCA, nontraumatic	Unresponsive	Prehospital cooling	No prehospital cooling	Survival at discharge	PEA/asys	Not specified	74	8	40	20%	2	34	6%	-14%	-29% to 1%
Debaty, 2014 ^{e39}	I	OHCA	Patients eligible for advanced life support	Intra-arrest cooling (prehospital cooling)	No prehospital cooling	Survival at discharge	All rhythms	Not specified	145	5	122	4.1%	7	123	5.7%	1.6%	-4.3% to 7.7%
Debaty, 2014 ^{e39}	I	OHCA	Patients eligible for advanced life support	Intra-arrest cooling (prehospital cooling)	No prehospital cooling	CPC 1-2	All rhythms	Not specified	145	4	122	3.3%	7	123	5.7%	2.4%	-3.2% to 8.4%
Kämäräinen, 2009 ^{e38}	I	OHCA	GCS ≤5	Prehospital cooling	No prehospital cooling	Survival at discharge	All rhythms	Not specified	37	8	18	44%	8	19	42%	2.3%	27.0% to 31.3%
Kämäräinen, 2009 ^{e38}	I	OHCA	GCS ≤5	Prehospital cooling	No prehospital cooling	CPC 1-2	All rhythms	Not specified	37	8	18	44%	8	19	42%	2.3%	27.0% to 31.3%
Drugs + TH																	
Damian, 2004 ^{e44}	II	OHCA, cardiac origin	"Coma with response to pain no better than flexion"	Coenzyme Q ₁₀ + TH	TH alone	Survival at discharge	Combined	Not specified	49	17	24	71%	21	25	84%	13%	-10% to 36%
Damian, 2004 ^{e44}	II	OHCA, cardiac origin	"Coma with response to pain no better than flexion"	Coenzyme Q ₁₀ + TH	TH alone	Survival at 3 mo	Combined	Not specified	49	7	24	29%	17	25	68%	39%	13%-65%
Damian, 2004 ^{e44}	II	OHCA, cardiac origin	"Coma with response to pain no better than flexion"	Coenzyme Q ₁₀ + TH	TH alone	GOS 4-5 at 3 mo	Combined	Not specified	49	5	24	21%	9	25	36%	15%	-10% to 40%
Cariou, 2008 ^{e45}	II	OHCA, cardiac origin	Persistent coma with GCS < 7	Epo 40,000 IU q12 4 doses + TH	TH alone	Mortality at 1 mo	Combined	Not specified	58	21	40	53%	8	18	44%	-8%	-36% to 20%
Cariou, 2008 ^{e45}	II	OHCA, cardiac origin	Persistent coma with GCS < 7	Epo 40,000 IU q12 4 doses + TH	TH alone	Survival at 1 mo	Combined	Not specified	58	19	40	48%	10	18	56%	8%	-20% to 36%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Standardized care																	
Hollenbeck, 2012 ^{e43}	III	OHCA, IHCA, nontraumatic	"unresponsive to commands or comatose after ROSC"	CODE ICE	Standard care	CPC 1-2 at discharge	Combined	Not specified	150	37	82	45%	25	68	37%	-8%	-24% to 7%
Hollenbeck, 2012 ^{e43}	III	OHCA, IHCA, nontraumatic	"unresponsive to commands or comatose after ROSC"	CODE ICE	Standard care	Survival to discharge	Combined	Not specified	150	38	82	46%	29	68	43%	-4%	-20% to 12%
Neuroprotective drugs																	
Brain Resuscitation Clinical Trial I Study Group, 1986 ^{e51}	I	OHCA, IHCA, almost any cause	"No purposeful motor response to pain after ROSC"	Thiopental single loading dose of 30 mg/kg	Standard therapy	CPC 1-2 at any time	NR	Not specified	262	43.4	131	33%	46	131	35%	2%	-9% to 13%
Brain Resuscitation Clinical Trial I Study Group, 1986 ^{e51}	I	OHCA, IHCA, almost any cause	"No purposeful motor response to pain after ROSC"	Thiopental single loading dose of 30 mg/kg	Standard therapy	Survival at 1 y	NR	Not specified	263	25.9	131	20%	30.2	132	23%	3%	-7% to 13%
Brain Resuscitation Clinical Trial I Study Group, 1986 ^{e51}	I	OHCA, IHCA, almost any cause	"No purposeful motor response to pain after ROSC"	Thiopental single loading dose of 30 mg/kg	Standard therapy	CPC 1-2 at 1 y	NR	Not specified	263	20	131	15%	26.1	132	20%	5%	-5% to 14%
Grafton, 1988 ^{e54}	III	OHCA (asys or VF)	"Patient not awake on admission"	Steroids, any dose	Did not receive steroids	Awakening at discharge	NR	Not specified	389	94	189	50%	115	200	58%	8%	-2% to 18%
Grafton, 1988 ^{e54}	III	OHCA (asys or VF)	"Patient not awake on admission"	Steroids, any dose	Did not receive steroids	Survival at discharge	NR	Not specified	389	88	189	47%	106	200	53%	6%	-3% to 16%
Jastremski, 1989 ^{e53}	II	OHCA, IHCA,	"Initially comatose"	Steroids, various doses	No steroids	CPC 1-2 at 1 y	NR	Not specified	261	24	70	34%	65	191	34%	0%	-13% to 13%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
		almost any cause		arbitrarily divided into 4 dose categories													
Jastremski, 1989 ^{e53}	II	OHCA, IHCA, almost any cause	"Initially comatose"	Steroids, various doses arbitrarily divided into 4 dose categories	No steroids	Survival at 1 y	NR	Not specified	261	10	70	14%	46	191	24%	10%	0%-20%
Roine, 1990 ^{e48}	I	OHCA, cardiac origin		Nimodipine bolus plus 0.5 µg/kg/min for 24 h	Placebo	Survival at 1 y	VF		155	29	80	36%	30	75	40%	4%	-12% to 19%
Roine, 1990 ^{e48}	I	OHCA, cardiac origin		Nimodipine bolus plus 0.5 µg/kg/min for 24 h	Placebo	GOS 5 at 1 y	VF		155	19	80	24%	22	75	29%	6%	-8% to 19%
Brain Resuscitation Clinical Trial II Study Group, 1991 ^{e49}	I	OHCA, IHCA, almost any cause	"No purposeful motor response to pain after ROSC"	Lidoflazine 1 mg/kg then 0.25 mg/kg at 8 and 16 h	Standard therapy	CPC 1-2 at any time	NR	Not specified	516	59.1	257	23%	61.9	259	24%	1%	-6% to 8%
Brain Resuscitation Clinical Trial II Study Group, 1991 ^{e49}	I	OHCA, IHCA, almost any cause	"No purposeful motor response to pain after ROSC"	Lidoflazine 1 mg/kg then 0.25 mg/kg at 8 and 16 h	Standard therapy	Survival at 6 mo	NR	Not specified	516	43.9	257	17%	47.9	259	19%	1%	-5% to 8%
Longstreth, 2002 ^{e52}	I	OHCA, nontraumatic	"Not awakened prior to randomization"	Magnesium 2 g, diazepam 10 mg boluses	Placebo	Survival at 3 mo	Combined	Not specified	300	42	150	28%	45	150	30%	2%	-8% to 12%

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Reisinger, 2009 ^{e50}	III	OHCA, IHCA, nontraumatic		Selenium 200-1,000 µg over 30 min once daily for 5 days	Placebo	CPC 1-2 within 6 mo	Combined	Not specified	226	40	102	39%	62	124	50%	11%	-2% to 24%
Reisinger, 2009 ^{e50}	III	OHCA, IHCA, nontraumatic	“unconscious and mechanically ventilated on admission to the intensive care unit”	Selenium 200-1,000 µg over 30 min once daily for 5 days	Placebo	CPC 1-3 within 6 mo	Combined	Not specified	226	49	102	48%	83	124	67%	19%	6%-32%
Reisinger, 2009 ^{e50}	III	OHCA, IHCA, nontraumatic	“unconscious and mechanically ventilated on admission to the intensive care unit”	Selenium 200-1,000 µg over 30 min once daily for 5 days	Placebo	Survival at discharge	Combined	Not specified	226	45	102	44%	70	124	56%	12%	-1% to 25%
Reisinger, 2009 ^{e50}	III	OHCA, IHCA, nontraumatic	“unconscious and mechanically ventilated on admission to the intensive care unit”	Selenium 200-1,000 µg over 30 min once daily for 5 days	Placebo	Survival at 6 mo	Combined	Not specified	226	36	102	35%	57	124	46%	11%	-2% to 23%
Kuisma, 2006 ^{e55}	I	OHCA, witnessed	No mention of level of consciousness but patients were intubated and mechanically ventilated	100% oxygen for 60 min post ROSC	30% oxygen	Survival at discharge	VF	Not specified	28	10	14	71%	10	14	71%	0%	-33% to 33%

Author, y	Classes	Population	Definition of coma	Intervention	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
Arola, 2013 ^{e47}	III	OHCA, cardiac origin	No response to verbal commands after ROSC and before randomization	Xenon 40% until rewarming + TH	TH	Mortality at discharge	VT/VF	Not specified	33	4	17	24%	3	16	19%	-5%	-33% to 23%
Arola, 2013 ^{e47}	III	OHCA, cardiac origin	No response to verbal commands after ROSC and before randomization	Xenon 40% until rewarming + TH	TH	Survival at discharge	VT/VF	Not specified	33	13	17	76%	13	16	81%	5%	-23% to 33%
Laitio, 2016 ^{e46}	I	Witnessed OHCA	"Comatose survivors"	Xenon 40% until rewarming + TH	TH	Mean global fractional anisotropy value	VT/VF	Based on poor neurologic status (serious HIE, resistant status epilepticus) (n=27) or septic multiorgan failure, cardiac failure (n=1 each). 29 patients total, 14 in xenon group and 15 in control group	110	Mean 0.433 (SD 0.028)			Mean 0.419 (SD 0.033)			Adjusted mean global fractional anisotropy value 3.8% higher in xenon group	1.1% to 6.4%
Laitio, 2016 ^{e46}	I	Witnessed OHCA	"Comatose survivors"	Xenon 40% until rewarming + TH	TJ	6-month mortality	VT/VF	As above	110	19	55	34.5%	15	55	27.3%	-7.3%	-24.0% to 9.8%
Laitio, 2016 ^{e46}	I	Witnessed OHCA	"Comatose survivors"	Xenon 40% until rewarming + TH	TJ	CPC	VT/VF	As above	110	Median 1 [IQR 1-5]			Median 1 [IQR 1-5]			Median difference 0	0-0, p=0.93

Comparing cooling methods

Author, y	Classes	Population	Definition of coma	Interventions	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
de Waard, 2013 ^{e42}	III	OHCA, IHCA	"Patient is unconscious at admission"	Continuous peritoneal lavage TH	Cool saline infusions and cooling blankets	Survival at discharge from ICU	Combined	Not specified	115	46	99	46%	11	16	69%	22%	-2% to 47%
37	III	OHCA, IHCA, cardiac origin	"persisting coma after successful resuscitation"	Invasive cooling	Surface cooling	CPC 1-2 at discharge	Combined	Not specified	78	14	39	36%	14	39	36%	0%	-21% to 21%
Pittl, 2013 ^{e41}	III	OHCA, IHCA, cardiac origin	"persisting coma after successful resuscitation"	Invasive cooling	Surface cooling	Survival to discharge	Combined	Not specified	78	21	39	54%	24	39	62%	8%	-14% to 30%
Medical Interventions																	
Kuisma, 2006 ^{e55}	I	Bystander witnessed OHCA, VF	(Comatose not listed as criterion, but O2 applied in immediate post-ROSC period)	100% O2 for a 60-minute period	30% O2 for a 60-minute period	Survival at hospital discharge	VF	Not specified	28	10	14	71%	10	14	71%	0%	-34% to 34%
Kuisma, 2006 ^{e55}	I	Bystander witnessed OHCA, VF	(Comatose not listed as criterion, but O2 applied in immediate post-ROSC period)	100% O2 for a 60-minute period	30% O2 for a 60-minute period	Good neurologic outcome	VF	Not specified	28	8	14	57%	6	14	43%	-14%	-51% to 22%
Laurent, 2005 ^{e56}	I	OHCA of presumed cardiac etiology	Exclusion criteria included response to verbal commands after ROSC	Isovolumic high-volume hemofiltration <i>without</i> mild hypothermia	Standard supportive care	6-month survival	Combined	Not specified	61 over 3 groups	4	19	21%	9	20	45%	24.0%	-5.5% to 48.2%
Laurent, 2005 ^{e56}	I	OHCA of presumed	Exclusion criteria included	Isovolumic high-volume hemofiltration	Standard supportive care	6-month survival	Combined	Not specified	61 over 3 groups	4	19	21%	7	22	32%	10.8%	-16.4%

Author, y	Class	Population	Definition of coma	Intervention	Control	Outcome	Group	WOLST	Total patients	Outcome control	Total control	Risk control	Outcome treatment	Total treatment	Risk treatment	Risk difference	95% CI
		cardiac etiology	response to verbal commands after ROSC	n with mild hypothermia													to 35.1%

Abbreviations: asys = asystole; CI = confidence interval; CPC = Cerebral Performance Category; Epo = epoetin alfa; GOS = Glasgow Outcome Scale; HIE = hypoxic ischemic encephalopathy; ICU = intensive care unit; IHCA = in-hospital cardiac arrest; NR = not reported; NT = normothermia; OHCA = out-of-hospital cardiac arrest; PEA = pulseless electrical activity; ROSC = return of spontaneous circulation; TH = therapeutic hypothermia; TTM = targeted temperature management; VF = ventricular fibrillation; VT = ventricular tachycardia; WOLST = withdrawal of life-support therapies.

Reference numbers of studies cited here taken from the complete guideline, published as a data supplement to the main article on Neurology.org.