

Supplement Table 41. Summary of clinical outcomes from randomized controlled trials evaluating micronutrient and antioxidant supplementation in critically ill adults (KQ16)

Nutrie nts	Study (year)	Group	No	Mortality			Infectious			Renal		LOS			MV		SOFA
				ICU	HOSP	28/30 d	INF.	BSI	PNEU/ VAP	AKI	RRT	ICU	HOSP	ICUFD	MVD	MVFD	Delta SOFA
Vit C	Duffy (2015) [196]	Vit C	13			0	2					2.3 (3.2)	8.8 (2.6)				
		Control	18			1	3					2.9 (3.5)	10.2 (4.8)				
	Zabet (2016) [197]	Vit C	14			2						21.45 (10.23)			1.53 (0.67)	1.95 (0.42)	
		Control	14			9						20.57 (13.04)					
	Emadi (2019) [198]	Vit C	25									1.22 (0.27)	4.12 (0.33)				
		Control	25									1.58 (1.18)	5.16 (3.44)				
	Fowler (2019) [199]	Vit C	84			25								10.7 (10.1)		13.3 (10.37)	-3 (3.4)
		Control	83			38								7.7 (9.6)		10.6 (9)	-2.7 (3.3)
	Wang (2020) [200]	Vit C	33	4		0			3	4		1.65 (0.98)	12.5 (3.7)				
		Control	37			0	3		6	5		1.65 (0.98)	14 (4.44)				
	Yanase (2020) [201]	Vit C	25	1	1					11		1.47 (1.48)	13.77 (9.11)				
		Control	25	0	0					13		1.77 (2.07)	12.43 (6.37)				
	El-Sherazy (2021) [202]	oral Vit C	21			4				1							-6 (3.53)
		Control	20			8				5							3 (3.38)
	Jamali Moghadam Siahkali (2021)[203]	Vit C	30		3							5.67 (5.9.3)	9.17 (3.7)				-8.73 (2.33)
		Control	30		3							5.33 (5.19)	7 (5.93)				-5.85 (2.61)
	Mahmoodpoor (2021) [204]	Vit C	40			6						12.77 (3.71)			4.05 (2.29)		
		Control	40			11						14.15 (3.12)			8.92 (2.96)		
	Zhang (2021) [205]	Vit C	29	6	6	6				3		22.9 (14.8)	35 (17)		1.5 (4.75)	21.67 (14.07)	
		Control	27	11	11	10				6		17.8 (13.3)	32.8 (17)		6 (4)	19.5 (14.44)	
	Kassem (2022) [206]	Vit C	40			13				4		8 (4.44)			4 (2.22)		
		Control	40			20				5		7 (4.44)			5 (2.22)		
	El Driny (2022) [207]	HD Vit C	20			3			1			9.33 (2.22)				22 (1.48)	-3.2 (2.8)
		LD Vit C	20			9			7			15.43 (12.37)				21.27 (1.26)	0.8 (3.3)
	Labbani-Motlagh (2022) [208]	Vit C	37			4				4							
		Control	37			6				10							
	Lamontagne (2022) [209]	Vit C	434			152				162							
		Control	429			137				164							
	Rosengrave (2022) [210]	Vit C	20		7	6						5.27 (5.63)	21.33 (17.78)				
		Control	20		7	7						10.07 (12.52)	28 (31.11)				
	Wacker (2022) [211]	Vit C	64	14		16					10	4.07 (4.22)	10.97(11.82)		20 (44.44)		
		Control	60	20		26					2	3.13 (2.81)	7.53 (6.44)		17.67 (35.56)		
	Adhikari (2023) [212]	Vit C	1037		395	361											-1.33 (2.96)
		Control	531		18	200											-2 (2.96)
	Anstey (2023) [213]	Vit C	35	7	11	10				1		4.67 (4.44)	13.33 (11.85)				
		Control	36	4	7	5				2		4.67 (2.96)	13.67 (9.63)				
	Belousoviene (2023) [214]	Vit C	12	7													
		Control	11	6													
	Vijayaraghavan (2023) [215]	Vit C	16			9				9							
		Control	14			6				6							
	Yanase (2023) [216]	Vit C	15	3	3	3	1				2		17.3 (15.56)	21 (5.93)			-0.32 (2.06)
		Control	15	1	1	1	3				0		14.3 (11.85)	23.3 (3.7)			1.11 (1.8)
	Karadžić Kočica	Vit C	75	1					13	1		32 (17.8)					

	(2024) [217]	Control	75	8					32	8		48 (17.8)					
	Li (2024) [218]	Vit C	20				0					17.3 (14.3)	20.8 (6.91)			7.2 (5.34)	-0.27 (0.24)
		Control	18				3					11.89 (6.85)	17 (5.55)			8 (9.04)	-0.27 (0.22)
	Privšek (2024) [219]	Vit C	18				11	4		2		2	5.08 (1.59)	15.3 (6.36)			0 (1.48)
		Control	12				5	5		1		1	8.75 (2.95)	14.2 (7.11)			1 (1.48)
	Zhao (2025) [220]	Vit C	109				3										
		Control	103				4										
Se	Andrews (2011) [221]	Se	251	84								14.48 (11.85)	31.68 (27.93)				
		Control	251	84								16.73 (14.89)	33.83 (31.63)				
	Manzanares (2011) [222]	Se	15	3			5			1	7	0	14 (11)			10 (8)	
		Control	16	5			7			6	8	0	13 (6)			9 (4)	
	Valenta (2011) [223]	Se	75			19											
		Control	75			24											
	Chelkeba (2015) [224]	Se	29				9			16			19.7 (11)	25.2 (10)		8.9 (5)	
		Control	25				10			21			23.8 (13)	24.5 (9)		10.7 (4.5)	
	Bloos (2016) [225]	Se	543				152	243					12.67 (12.59)	28 (19.26)			2.33 (3.7)
		Control	546				137	269					14 (13.33)	32 (24.44)			2.33 (3.7)
	Chelkeba (2017) [226]	Se	29				9				5						
		Control	25				10				7						
	Moghaddam (2017) [227]	Se	57			9							14.51 (8.01)	19.4 (8.76)		8.44 (8.09)	-4.4 (2.7)
		Control	56			11							15.91 (13.24)	20.04 (13.14)		9.3 (11.2)	-2.8 (2.9)
	Schmidt (2018) [228]	Se	206				8				13		2.04 (3.08)	12 (5)			
		Control	205				5				17		2.33 (2.58)	14 (11)			
	Mahmoodpoor (2019) [229]	Se	20			11								16.6 (7.8)		13.2 (6.7)	-3.2 (2.3)
		Control	20			16								18.5 (7.7)		14.9 (6.9)	-3.3 (2.4)
	Laaf (2022) [230]	Se	10	2	2	2	5	3		5	3		23.7 (21.5)	41.3 (27.4)		12.33 (17.68)	
		Control	10	1	1	1	5	1		4	0		16.7 (5.9)	33.7 (20.7)		10.54 (10.65)	
	Stoppe (2023) [231]	Se	697				29	62					2.83 (3.04)	10.03 (6.59)			
		Control	697				35	58					2.77 (2.89)	9.67 (6.07)			
Vit D	Leaf (2014) [232]	Calcitriol	36	7	8	6					1	10.33 (9.63)	23.67 (11.11)			22 (11.11)	
		Control	31	6	7	7					1	11.67 (7.41)	22 (11.11)			18 (15.56)	
	Ginde (2019) [233]	Vit D	538	92	92			20			199	20		9.1 (9.2)		21.3 (11.3)	
		Control	540	72	69						198	18		10.4 (11)		22.1 (10.5)	
	Bychinin (2022) [234]	Vit D	52		19		31	23					15.2 (10.4)	22.8 (13.3)		15 (5.9)	
		Control	54		27		22	13					8.3 (9.6)	15.8 (9.6)		10.2 (9.3)	
	Domazet Bugarin (2023) [235]	Vit D	75				23	56					14 (8.15)	19.6 (8.7)		10.33 (6.67)	
		Control	77				27	55					13.33 (8.89)	18.33 (9.63)		9.67 (6.67)	
	Ashoor (2024) [236]	HD Vit D	37				3			0			15.9 (3.9)	19.8 (4)		12.8 (3.8)	
		LD Vit D	38				9			6			17.8 (5.8)	26.1 (5.6)		14.6 (4.7)	
Thiamine	Andersen (2016) [237]	Thiamine	31		0		5				1		2.57 (2.3)	5.67 (2.96)			
		Control	33		1		5				2		2.57 (1.93)	5.33 (2.22)			
	Donnino (2016) [238]	Thiamine	45		18						1		8.33 (6.67)	13.67 (8.89)			
		Control	43		20						8		9.33 (11.11)	14.67 (12.59)			
	Harun (2019) [239]	Thiamine	32	14									6.67 (5.19)				-3 (3.4)
		Control	33	12									7 (6.67)				-2.7 (3.3)
	Petsakul (2020) [240]	Thiamine	25				5										-3.42 (3.15)
		Control	25				7										-3.92 (3.52)
	Moslemi (2020) [241]	Thiamine	48													1.8 (1.9)	
		Control	48													2.14 (0.89)	
	Moskowitz (2023)	Thiamine	42		15						23	6			15.83		

NAC	[242]													(18.52)			
		Control	46		25				34	10				7.67 (17.04)			
	Donnino (2024) [243]	Thiamine	40		30	30											
		Control	36		23	24											
	Najafi (2014) [244]	NAC	21	8							21.2 (20.71)			19.82 (19.55)			
		Control	18	4							27.72 (39.46)			13.82 (11.69)			
	Hamamsy (2019) [245]	NAC IV	30								5.4 (1.2)	9.1 (3.2)					
		Control	30								5.7 (1.6)	11.4 (5.8)					
	Taher (2021) [246]	NAC	47			12				3	9 (5.19)	15 (15.56)				17.4 (12.6)	
		Control	45			14				4	11 (8.15)	17 (14.81)				16.6 (13)	
Others	Gamarra-Morales (2023) [247]	NAC	72			25					26.2 (25.5)			24.6 (23.1)			
		Control	68			28					22.1 (19.1)			20.7 (16.2)			
	Rahimi (2023) [248]	NAC	20		10						12.9 (6.49)	14.65 (6.66)					
		Control	20		15						13.95 (7.1)	16.3 (7.42)					
	Heyland (2013) [249]	AOX	617		216	190	168	64	71	72	9.7 (5.86)	20.63 (10.38)				2.7(2.6)	
		Control	601		199	173	181	54	95	62	9.78 (5.65)	19.47 (9.91)				2.7(2.7)	
	Hejazi (2018) [250]	ALA	37	3	8	4					14.57 (10.59)	27.57 (20.52)				5.17 (5.26)	
		Control	35	5	8	6					18.23 (15.7)	28.4 (21.33)				5.23 (7.93)	
	Cherukuri (2019) [251]	Vit A	32			11		7			6 (1.0)			6.3 (1.5)			
		Control	32			9		7			7.9 (1.1)			4.5 (1)			
	Hasanloei (2021) [252]	coEnz Q10	20								9.4 (3.26)	13.2 (7.65)		6.85 (2.58)			-3.05 (1.32)
		Control	20								13.35 (5.55)	19.15 (8.46)		9.8 (4.05)			-1.3 (0.66)
	Yahyapoor (2022) [253]	L-carnitine	24			7					13.2 (4.3)	20.2 (14.75)		10.66 (5.25)			
		Control	27			16					18.33 (15.54)	27.37 (19.33)		17.14 (14.41)			
	Zhong(2022) [254]	ALA	9			3											
		Control	8			7											
	Patel (2023) [255]	HCA	10	3	4					3				10.33 (15.56)		12.33 (18.52)	
		Control	10	4	4					3				7.67 (12.59)		10 (13.33)	
	Kim(2023) [256]	NAC + Se	53						4		8.9 (0.71)	22.4 (1.66)					
		Control	50						6		11.6 (0.95)	24.2 (1.45)					
	Majidi (2024) [257]	Vit B com.	40			33					10 (8.17)						
		Control	45			43					4.83 (3.84)						
	Aghasadeghi (2024) [258]	Spirulina	47		0						8 (1.48)	11.67 (2.22)					
		Control	52		15						7.67 (2.22)	11.97 (2.44)					
	Makiabadi (2024) [259]	Vit E + Zinc	40			0					3.64 (0.97)	6.9 (1.1)					
		Control	38			2					5.23 (3.88)	8.9 (4.4)					

Values are presented as number of events or mean (standard deviation).

ICU, intensive care unit; HOSP, hospital; INF, infection; BSI, blood stream infection; PNEU, pneumonia; VAP, ventilator associated pneumonia; AKI, acute kidney injury; RRT, renal replacement therapy; LOS, length of stay; ICUFD, ICU free days; MV, mechanical ventilation; MVD, mechanical ventilation days; MVFD, MV free days; SOFA, sequential organ failure assessment; Vit C, vitamin C; HD, high dose; LD, low dose; Se, selenium; Vit D, vitamin D; NAC, n-acetylcysteine; Vit A/B, vitamin A/B; com, complex; coEnz, coenzyme; ALA, alpha-lipoic acid; HCA, hydroxocobalamine.

