## **SUPPLEMENTAL DIGITAL CONTENT 17**

(unpublished)

This table also appears in the Supplemental Digital Content 2 in the complete set of evidence tools.

### Table 73. Selenium supplement compared to no selenium in sepsis or septic shock

Author(s): Jones A, Alhazzani W
Date: April 13, 2016
Question: Selenium supplement compared to no selenium in sepsis or septic shock
Setting: ICU
Bibliography: Alhazzani W, Jacobi J, Sindi A, Hartog C, Reinhart K, Kokkoris S, Gerlach H, Andrews P, Drabek T, Manzanares W, Cook DJ. The effect of selenium therapy on mortality in patients with sepsis syndrome: a systematic review and meta-analysis of randomized controlled trials. Critical care medicine. 2013 Jun 1;41(6):1555-64.; Bloos F, Trips E, Nierhaus A, Briegel J, Heyland DK, Jaschinski U, Moerer O, Weyland A, Marx G, Gründling M, Kluge S. Effect of Sodium Selenite Administration and Procalcitonin-Guided Therapy on Mortality in Patients With Severe Sepsis or Septic Shock: A Randomized Clinical Trial. JAMA internal medicine. 2016 Sep 1;176(9):1266.

studies         design         bias           Mortality (hospital or if not reported ICU/28 days mortality)	Imprecision         Other considerations           serious <sup>2</sup> none	Selenium supplement 288/906 (31.8%)	no selenium 305/916 (33.3%) <sup>3</sup>	Relative (95% CI) OR 0.94 (0.77 to	Absolute (95% CI) 14 fewer		CRITICAL
10 randomized serious not serious not serious se	serious <sup>2</sup> none		-			⊕⊕◯◯	CRITICAL
	serious <sup>2</sup> none		-			$\Theta \Theta O O$	CRITICAL
			20.0%	1.15)	<b>per 1000</b> (from 32 more to 55 fewer) <b>10 fewer</b> <b>per 1000</b> (from 23 more to 39 fewer)	LOW	

3	randomized trials	not serious	not serious	not serious	serious <sup>4</sup>	none	197/641 (30.7%)	179/640 (28.0%)	<b>OR 1.14</b> (0.89 to 1.45)	<b>27 more</b> <b>per 1000</b> (from 23 fewer to 81 more)	DDD MODERATE	CRITICAL
Nosocom	nial Pneumonia											
3	randomized trials	serious <sup>5</sup>	not serious <sup>6</sup>	not serious	very serious <sup>7</sup>	none	28/135 (20.7%)	28/136 (20.6%) 10.0%	OR 0.83 (0.28 to 2.49)	29 fewer per 1000 (from 138 fewer to 186 more) 16 fewer per 1000 (from 70 fewer to 117 more)	⊕ VERY LOW	IMPORTANT
ICU lengt	th of stay					-						•
3	randomized trials	serious <sup>5</sup>	not serious	not serious	serious <sup>8</sup>	none	668	681	-	MD <b>0.12</b> days lower (1.42 lower to 1.17	⊕⊕⊖⊖ Low	IMPORTANT

MD – mean difference, RR – relative risk

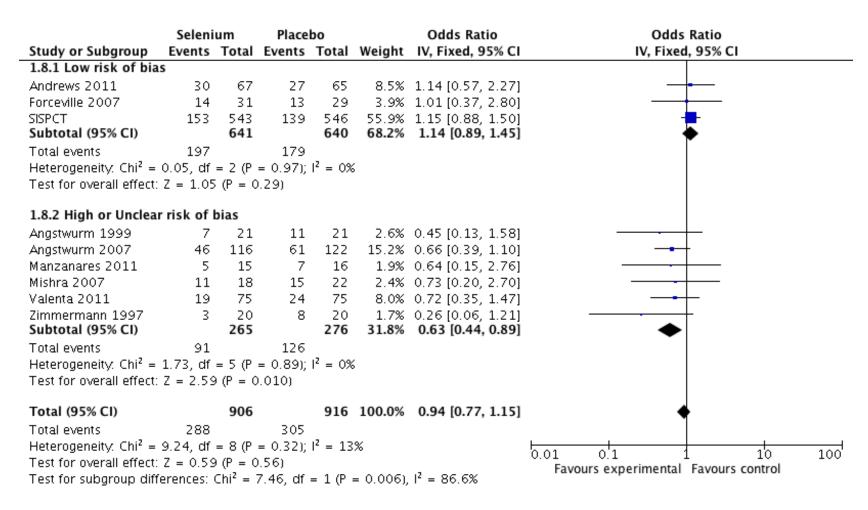
- 1. We downgraded the quality of evidence by one level for risk of bias, three studies were at high risk of bias, mainly due to lack of blinding (detection and performance biases) and incomplete outcome data (attrition bias), and four studies were classified as unclear risk of bias.
- 2. We downgraded the quality of evidence by one level for imprecision, the results were sensitive to the metric used to summarize the results, if RR is used the UL of CI reaches 1, therefore we decided to lower the quality of evidence
- 3. estimates of mortality from sepsis is approximately 20% (Kaukonen KM, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA. 2014;311(13):1308-16.)
- 4. We downgraded the quality of evidence for imprecision by one level, the CI contained small benefit but significant harm (45% relative risk increase in mortality)
- 5. We downgraded the quality if evidence for risk of bias by one level.
- 6. Although  $I^2 = 50\%$  we did not downgrade for imprecision, because we downgraded for other categories
- 7. We downgraded the quality of evidence by two levels for imprecision, the CI was very wide including substantial benefit and harm
- 8. We downgraded the quality of evidence for imprecision by one level

# Figure 61. Selenium compared to placebo in septic patients: Mortality Outcome

Study or Subgroup	Seleni Events		Place Events		Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% Cl
Andrews 2011	30	67	27	65	7.6%		
Angstwurm 1999	7	21	11	21	3.7%	0.45 [0.13, 1.58]	
Angstwurm 2007	46	116	61	122	18.0%	• • •	
Forceville 2007	14	31	13	29	3.7%	. , .	
Manzanares 2011	5	15	7	16	2.3%		
Mishra 2007	11	18	15	22	2.6%	0.73 [0.20, 2.70]	
SISPCT	153	543	139	546	49.8%	1.15 [0.88, 1.50]	+
Valenta 2011	19	75	24	75	9.0%	0.72 [0.35, 1.47]	
Zimmermann 1997	3	20	8	20	3.4%	0.26 [0.06, 1.21]	
Total (95% CI)		906		916	100.0%	0.94 [0.77, 1.15]	
Total events	288		305				
Heterogeneity: Chi <sup>2</sup> =	9.24, df	= 8 (P	= 0.32);	$ ^2 = 13$		0.02 0.1 1 10 50	
Test for overall effect:	Z = 0.62	(P = 0)	Favours Selenium Favours Placebo				

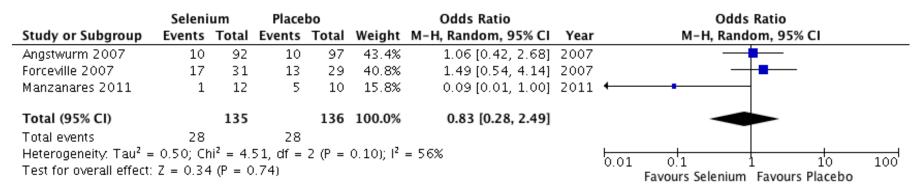
M-H: Mantel-Haenszel

Figure 62. Selenium compared to placebo in septic patients: Mortality Outcome Split by risk of bias of underlying studies.



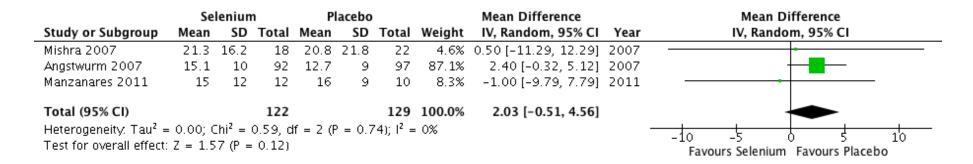
**IV:** Inverse variance

### Figure 63. Selenium compared to placebo in septic patients: Pneumonia Outcome



M-H: Mantel-Haenszel

### Figure 64. Selenium compared to placebo in septic patients: ICU length of stay Outcome



**IV:** Inverse variance