

**Table S5** Effects on the levels of B vitamin concentrations

CI – Confidence Interval; NR – Not Reported; SD – Standard Deviation. \* In few publications for folate level, the unit reported was in nmol/L and for Vitamin B12 pmol/L. Therefore, for maintaining the consistency the values were converted in ng/mL and pg/mL for folate and Vitamin B12 respectively. Those results are indicated with (\*).

Author and year	Intervention/comparator	n	Time point	B vitamin concentrations	% change to baseline	p-value
<b>Folate level (ng/mL)</b>						
Kwok, 2020 (52)	Vitamin B <sub>12</sub> + folic acid	138	Baseline	Mean (SD): 12.2 (3.5)*	-	NR
	Placebo	141		Mean (SD): 12.9 (3.7)*	-	
	Vitamin B <sub>12</sub> + folic acid	121	12 months	Mean (SD): 19.1 (2.0)*	<b>56.6%</b>	<b>&lt; 0.0001</b>
	Placebo	125		Mean (SD): 12.7 (3.6)*	-1.6%	
	Vitamin B <sub>12</sub> + folic acid	118	24 months	Mean (SD): 21.1 (5.5)*	<b>73.0%</b>	<b>&lt; 0.0001</b>
	Placebo	120		Mean (SD): 12.2 (4.3)*	-5.4%	
Ma, 2019a (17)	Folic acid alone	60	Baseline	Mean (SD): 7.71 (1.17)	-	NR
	Vitamin B <sub>12</sub> alone	60		Mean (SD): 7.55 (0.13)	-	
	Vitamin B <sub>12</sub> + folic acid	60		Mean (SD): 7.71 (0.26)	-	
	Control	60		Mean (SD): 7.61 (0.6)	-	
	Folic acid alone	60	6 months	Mean (SD): 9.71 (0.11)	<b>25.9%</b>	<b>0.009</b>
	Vitamin B12 alone	60		Mean (SD): 8.24 (0.37)	<b>9.1%</b>	
	Vitamin B <sub>12</sub> + folic acid	60		Mean (SD): 9 (0.57)	<b>16.7%</b>	
	Control	60		Mean (SD): 9.58 (1.56)	25.9%	
Ma, 2019b (19)	Folic acid supplementation	90	Baseline	Mean (SD): 7.01 (0.64)	-	NR
	Control	90		Mean (SD): 5.79 (0.67)	-	

Author and year	Intervention/comparator	n	Time point	B vitamin concentrations	% change to baseline	p-value
	Folic acid supplementation	90	6 months	Mean (SD): 8.97 (0.62)	28.0%	NR
	Control	90		Mean (SD): 5.97 (2.11)	3.1%	
	Folic acid supplementation	90	12 months	Mean (SD): 9.44 (0.33)	34.7%	NR
	Control	90		Mean (SD): 5.88 (0.53)	1.6%	
	Folic acid supplementation	90	18 months	Mean (SD): 9.51 (0.39)	35.7%	NR
	Control	90		Mean (SD): 5.89 (0.42)	1.7%	
	Folic acid supplementation	90	24 months	Mean (SD): 9.94 (0.37)	<b>41.8%</b>	<b>0.042</b>
	Control	90		Mean (SD): 5.83 (0.43)	0.7%	
Blasko, 2012 (35)	Non user	51	Baseline	Mean (SD): 8.4 (3.6)	-	NR
	Inconsistent users	20		Mean (SD): 9.4 (5.1)	-	
	Combination users	10		Mean (SD): 12.9 (7.2)	-	
	Non user	51	60 months	Mean (SD): 8.5 (4.3)	1.2%	NR
	Inconsistent users	20		Mean (SD): 14.7 (8.5)	<b>56.4%</b>	<b>0.024</b>
	Combination users	10		Mean (SD): 18.4 (6)	<b>42.6%</b>	<b>&lt;0.000</b>
De Jager, 2012 (53)	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	110	Baseline	Mean (95%CI): 9.9 (8.8-11.2)*	-	NR
	Placebo	113		Mean (95%CI): 10.1 (9.0-11.4)*	-	
	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	110	24 months	Mean (95%CI): 36.9 (32.7-41.7)*	<b>272.7%</b>	<b>&lt;0.001</b>
	Placebo	113		Mean (95%CI): 10.9 (9.6-12.3)*	7.9%	NR
Schroecksnadel, 2006 (51, 54)	Vitamin B <sub>1</sub> , B <sub>6</sub> , B <sub>12</sub> , and folic acid	15	Baseline	Mean (SD): 6.9 (2.3)	-	NR
		15	1 month	Mean: 27.76	<b>302.3%</b>	<b>&lt;0.01</b>
Lehmann, 2003 (32)	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	30	Baseline	Mean (SD): 5.5 (3.1)*	-	NR
		30	9 months	Mean (SD): 17.6 (0)*	<b>220.0%</b>	<b>&lt;0.00001</b>
<b>Vitamin B12 (pg/mL)</b>						
Kwok, 2020 (52)	Vitamin B <sub>12</sub> + folic acid	138	Baseline	Mean (SD): 115.8 (40.3)*	-	NR
	Placebo	141		Mean (SD): 116.2 (44.5)*	-	

Author and year	Intervention/comparator	n	Time point	B vitamin concentrations	% change to baseline	p-value
	Vitamin B <sub>12</sub> + folic acid	121	12 months	Mean (SD): 169.6 (13.4)*	<b>46.5%</b>	<b>&lt; 0.0001</b>
	Placebo	125		Mean (SD): 117.6 (43.1)*	1.2%	NR
	Vitamin B <sub>12</sub> + folic acid	118	24 months	Mean (SD): 167.5 (18.4)*	<b>44.6%</b>	<b>&lt; 0.0001</b>
	Placebo	120		Mean (SD): 116.2 (46)*	0.0%	NR
Ma, 2019a (17)	Folic acid alone	60	Baseline	Mean (SD): 398.32 (5.59)	-	NR
	Vitamin B <sub>12</sub> alone	60		Mean (SD): 403.65 (9.97)	-	
	Vitamin B <sub>12</sub> + folic acid	60		Mean (SD): 401.02 (4.49)	-	
	Control	60		Mean (SD): 405.77 (5.15)	-	
	Folic acid alone	60	6 months	Mean (SD): 478.68 (14.76)	<b>20.2%</b>	<b>0.022</b>
	Vitamin B <sub>12</sub> alone	60		Mean (SD): 537.06 (5.58)	<b>33.1%</b>	<b>0.022</b>
	Vitamin B <sub>12</sub> + folic acid	60		Mean (SD): 491.96 (13.28)	<b>22.7%</b>	<b>0.009</b>
	Control	60		Mean (SD): 406.09 (17.13)	0.1%	NR
Ma, 2019b (19)	Folic acid supplementation	90	Baseline	Mean (SD): 571.25 (23.37)	-	NR
	Control	90		Mean (SD): 568.48 (16.33)	-	NR
	Folic acid supplementation	90	6 months	Mean (SD): 583.78 (25.44)	2.2%	NR
	Control	90		Mean (SD): 537.43 (27.39)	-5.5%	NR
	Folic acid supplementation	90	12 months	Mean (SD): 571.33 (20.45)	0.0%	NR
	Control	90		Mean (SD): 555.45 (19.58)	-2.3%	NR
	Folic acid supplementation	90	18 months	Mean (SD): 574.33 (20.13)	0.5%	NR
	Control	90		Mean (SD): 561.22 (19.53)	-1.3%	NR
	Folic acid supplementation	90	24 months	Mean (SD): 575.26 (19.31)	0.7%	0.069
	Control	90		Mean (SD): 569.44 (17.21)	0.2%	NR
Blasko, 2012 (35)	Non user	51	Baseline	Mean (SD): 479 (242)	-	NR
	Inconsistent users	20		Mean (SD): 752 (593)	-	NR
	Combination users	10		Mean (SD): 616 (174)	-	NR
	Non user	51	60 months	Mean (SD): 457 (205)	-4.6%	NR

Author and year	Intervention/comparator	n	Time point	B vitamin concentrations	% change to baseline	p-value
	Inconsistent users	20		Mean (SD): 712 (600)	-5.3%	0.024
	Combination users	10		Mean (SD): 564 (143)	<b>-8.4%</b>	<b>&lt;0.000</b>
De Jager, 2012 (53)	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	110	Baseline	Mean (95% CI): 449.9 (420.1-482.5)*	-	NR
	Placebo	113		Mean (95% CI): 439.1 (410.6-470.3)*	-	NR
	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	110	24 months	Mean (95% CI): 935.2 (872.8-1002.9)*	<b>107.9%</b>	<b>&lt;0.001</b>
	Placebo	113		Mean (95% CI): 471.6 (441.8-505.5)*	7.4%	NR
Schroecksnadel, 2006 (51, 54)	Vitamin B <sub>1</sub> , B <sub>6</sub> , B <sub>12</sub> , and folic acid	15	Baseline	Mean (SD): 489 (74.3)	-	NR
		15	1 month	Mean: 670.21	37.1%	Not sig
Lehmann, 2003 (32)	Vitamin B <sub>6</sub> , B <sub>12</sub> , and folic acid	30	Baseline	Mean (SD): 474.3 (181.6)*	-	NR
		30	9 months	Mean (SD): 1343.1 (257.5)*	<b>183.2%</b>	<b>&lt;0.00001</b>

CI – Confidence Interval; NR – Not Reported; SD – Standard Deviation. \* In few publications for folate level, the unit reported was in nmol/L and for Vitamin B12 pmol/L. Therefore, for maintaining the consistency the values were converted in ng/mL and pg/mL for folate and Vitamin B12 respectively. Those results are indicated with (\*).