Table S1. Studies that met inclusion criteria and are included in the qualitative analysis and eligible for the meta-analysis

Reference	Type of Study	Population Characteristics[3]	Intervention	Biomarker	Blood assay method[4]	Timing of exposure *Level/type of folate*	Serum/Plasma folate (nmol/L)	RBC folate (nmol/L)	Dietary folate intake (µg/d)
Aarabi, M. 2015 [1]	Dietary intervention trial	30 infertile men Age: 37.9± 1.3[5] Montreal, Canada 2009-2011	5mg of FA/d for 6 mo	RBC folate	Microbiologic - *L. casei*	**Baseline:** 5000 µg FA (n=28)	Unavailable	273 ± 24[6]	Unavailable
						Intervention: 24 wks 5000 µg FA (n=19)	Unavailable	488 ± 35[6]	Unavailable
Adank, C. 2003 [2]	Randomized control trial	138 healthy women Age: 18-40[7] Dunedin, New Zealand July - Oct 2000	**Intervention:** FA supplement feeding study (12 wks) Dietary questionnaire at baseline only	Plasma and RBC folate	Microbiologic - *L. casei*	**Baseline:** 400 µg/d FA: (n=36) 2800 µg/wk FA: (n=41)	19.7 ± 10.0[5] 22.9 ± 13.0[5]	645 ± 211[5] 624 ± 177[5]	223 (201, 246)[8] 260 (227, 292)[8]
						Intervention: 12 wks 400 µg/d FA: (n=36) 2800 µg/wk FA: (n=41)	Unavailable	1095 ± 295[5] 913 ± 225[5]	Unavailable
Amatayakul, K. 1984 [3]	Randomized controlled trial	67 healthy nonpregnant women Age: 18-35[7]	300 µg FA/d or placebo for 1 yr	Serum and RBC folate	Microbiologic - *L. casei*	**Baseline:** 300 µg FA/d (n=33)	24.3 ± 9.1[5,9]	706 ± 199.8[5,9]	Unavailable
						Intervention: 15 wks 300 µg FA/d (n=33)	37.5 ± 10.1[5,9]	944.3 ± 217.9[5,9]	Unavailable
						Intervention: 27 wks 300 µg FA/d (n=33)	37.7 ± 10.0[5,9]	957.9 ± 208.8[5,9]	Unavailable
						Intervention: 48 wks 300 µg FA/d (n=33)	38.4 ± 11.7[5,9]	1023.8 ± 227.0[5,9]	Unavailable
Anderson, C. 2010 [4]	Randomized control trial	107 healthy males and females Age: 60-90[7]	100 µg FA/d, 400 µg FA/d, 1000 µg FA/d, or 2000 µg FA/d for 6 wks	Serum folate	Radio-protein binding Quantaphase II (Bio-Rad Laboratories, Hercules, California)	**Baseline:** 100 µg/d FA: (n=27) 400 µg/d FA: (n=27) 1000 µg/d FA: (n=26) 2000 µg/d FA: (n=27)	10.9 (8.4 - 15.2)[8,9] 15.2 (8.4 - 18.4)[8,9] 13.6 (9.3 - 17.5)[8,9] 15.0 (12.3 - 17.9)[8,9]	Unavailable	244 (195-309)[8] 289 (221-341)[8] 281 (206-364)[8] 302 (184-388)[8]
						Intervention: 6 wks 100 µg FA/d (n=27) 400 µg FA/d (n=27) 1000 µg FA/d (n=26) 2000 µg FA/d (n=27)	15.9 (12.3 - 21.3)[8,9] 28.1 (21.8 - 37.9)[8,9] 36.5 (28.1 - 74.0)[8,9] 37.3 (24.3 - 148.7)[8,9]	Unavailable	Unavailable

Anderson, C. 2013 [5]	Randomized, double blind, crossover, control trial	235 randomized male and females; 142 anaylzed Age: 18-69[7] Seattle, WA, 1998-2001	0, 200, or 400 µg FA/d 2 12 wks supplementation intervention with a 30 wk washout period in between (AWO)	Serum and RBC folate	***From Author directly:*** ***Abbott IMx folate assay (ion capture assay) for Serum folate and RBC folate. In May 1999 when the Abbott Labs no longer used the IMx we switched to using the Beckman Access method***	**Baseline:** **Group B:** 200 µg first (n=34) **Group C:** 200 µg first (n=34) **Group A:** 200 µg AWO (n=42) **Group D:** 200 µg AWO (n=32) **Group D:** 400 µg first (n=32) **Group C:** 400 µg AWO (n=34) **Intervention: 6wks** **Group B:** 200 µg first (n=34) **Group C**: 200 µg first (n=34) **Group A**: 200 µg AWO (n=42) **Group D:** 200 µg AWO (n=32) **Group D:** 400 µg first (n=32) **Group C**: 400 µg AWO (n=34) **Intervention: 12 wks** **Group B**: 200 µg first (n=34) **Group C:** 200 µg first (n=34) **Group A**: 200 µg AWO (n=42) **Group D:** 200 µg AWO (n=32) **Group D:** 400 µg first (n=32) **Group C:** 400 µg AWO (n=34)	 $31.3 \pm 1.04^{6,9}$ $32.5 \pm 0.86^{6,9}$ $26.8 \pm 0.95^{6,9}$ $25.0 \pm 1.11^{6,9}$ $31.6 \pm 1.11^{6,9}$ $25.7 \pm 1.07^{6,9}$ $33.8 \pm 1.04^{6,9}$ $34.1 \pm 0.75^{6,9}$ $35.2 \pm 1.73^{6,9}$ $31.1 \pm 1.61^{6,9}$ $35.9 \pm 1.97^{6,9}$ $40.0 \pm 4.63^{6,9}$ $33.8 \pm 0.86^{6,9}$ $32.9 \pm 0.77^{6,9}$ $36.8 \pm 3.04^{6,9}$ $32.2 \pm 1.63^{6,9}$ $36.6 \pm 1.63^{6,9}$ $45.4 \pm 3.84^{6,9}$	 n/a[10] n/a[10] n/a[10]	 Unavailable Unavailable Unavailable
Ashfield-Watt, P. 2001 [6]	Randomized control trial	45 participants Age: 18-70[7]	250 µg FA/d for 3 months	Plasma folate	Competitive protein binding assay, Abbott IMX methods	**Baseline:** 250 µg FA (n=50) **Intervention: 3 mo** 250 µg FA (n=45)	 $12.7 \pm 4.5^{5,9}$ $19.5 \pm 8.4^{5,9}$	 Unavailable Unavailable	 Unavailable Unavailable
Ashfield-Watt, P. 2002 [7]	Crossover, dietary intervention trial	126 healthy subjects Age: 20-63[7]	400 µg FA/d for 4 months	Plasma folate	Competitive protein binding assay (Abbott IMX)	**Baseline:** 352 µg FA/d (n=126) **Intervention: 4 mo** 352 µg FA/d (n=108)	 17.7 ± 7.7^{5} 31.7 ± 16.5^{5}	 Unavailable Unavailable	 214 ± 70^{5} 201 ± 63^{5}
Baro, L. 2003 [8]	Dietary intervention trial	30 residents in Spain Age: 20-45[7]	drank 500 ml/d of semi-skimmed milk for 4 weeks (depletion) followed by 8 weeks of enriched semi-skimmed milk at 500 ml/d (150 µg FA/d)	Plasma folate	Immunoassay, SimulTRANC-SNB Radioassay Kit (ICN Pharmaceuticals, USA)	**Baseline:** 150 µg FA/d (n=30) **Intervention: 4 wks** 150 µg FA/d (n=30)	 $7.6 \pm 0.8^{6,9}$ $12.7 \pm 1.0^{6,9}$	 Unavailable Unavailable	 Unavailable Unavailable

						Intervention: 8 wks 150 µg FA/d (n=30)	13.8 ± 1.0[6]	Unavailable	Unavailable
Baro, L. 2004 [9]	Dietary intervention trial	31 healthy non-pregnant women Age: 21 – 37[7] Guatemala	400 µg FA/d from fortified dairy products for 8 wks	Plasma folate	Immunoassay, SimulTRANC-SNB Radioassay Kit (ICN Pharmaceuticals, USA)	**Baseline:** 400 µg/d FA (n=31)	8.6 ± 0.9[6]	Unavailable	Unavailable
						Intervention: 8 weeks 400 µg/d FA (n=31)	21.0 ± 1.4[6]	Unavailable	Unavailable
Basoglu, C. 2009 [10]	Randomized controlled trial	35 patients with depression Age: 18-66[7]	2500 µg FA/d for 6wks +Escitalopram	Serum folate	Electro-chemoluminescence immunoassay	**Baseline:** 2500 µg FA/d (n=20) + Escitalopram	12.3 (5.7, 23.2)[9,11]	Unavailable	Unavailable
						Intervention: 6 wks 2500 µg FA/d (n=20) + Escitalopram	15.9 (8.4, 45.4)[9,11]	Unavailable	Unavailable
Biswas, A. 2009 [11]	Dietary intervention trial	24 stroke patients Age: under 40 Northern India	5000 µg FA/d for 12 wks	Serum folate	Radioimmunoassay, Immulite (Diagnostic Product Corporation, Erlangen, Germany)	**Baseline:** 5000 µg FA/d (n=24)	11.2 (8.1, 14.2)[11]	Unavailable	Unavailable
						Intervention: 12 wks **50**00 µg FA/d (n=24)	11 (8.2, 14.2)[11]	Unavailable	Unavailable
Bramswig, S. 2009 [12]	Double-blind, placebo controlled intervention	46 healthy females Age:18-35[7] Germany	Intervention: daily multivitamin 800 µg FA for 16 weeks	RBC and Plasma folate	Microbiologic - *L. casei*	**Baseline:** 800 µg/d FA (n=21)	20.6 ± 5.8[5]	653.6 ± 37.0[6]	287 ± 99[5]
						Intervention: 4 wks 800 µg/d FA (n=21)	50.2 ±15.6[5]	917.9 ± 49.1[6]	Unavailable
						Intervention: 8 wks 800 µg/d FA (n=21)	72.2 ± 18.1[5]	1166.2 ± 46.7[6]	226 ± 89[5]
						Intervention: 12 wks 800 µg/d FA (n=21)	75.4 ± 21.4[5]	1339.4 ± 54.2[6]	Unavailable
						Intervention: 16 wks 800 µg/d FA (n=21)	77.6 ± 23.0[5]	1430.2 ± 53.1[6]	246 ± 97[5]
Bronstrup, A. 1998 [13]	Dietary intervention trial	150 women Age: 20-34[7]	400 µg FA/d, 400 µg FA/d + 6µg vit B-12/d, or 400 µg FA/d + 400 µg vit B-12/d	Plasma folate	Chemiluminescent (Chiron Diagnostics, Fernwald, Germany)	**Baseline:** 400 µg FA/d (n=51) 400 µg FA/d + 6 µg Vit B-12 (n=49) 400 µg FA/d + 400 µg Vit B-12 (n=50)	30.5 ± 10.2[5] 31.3 ± 12.9[5] 28.8 ± 8.6[5]	Unavailable	Unavailable
						Intervention: 4wks 400 µg FA/d (n=51) 400 µg FA/d + 6 µg Vit B-12 (n=49) 400 µg FA/d + 400 µg Vit B-12 (n=50)	46.6 ± 17.4[5] 46.1 ± 13.4[5] 44.0 ± 11.4[5]	Unavailable	Unavailable
Brouwer, I. 1998 [14]	Dietary intervention trial	44 healthy participants Age:18-45[7]	low folate diet plus 250 µg FA/d for 4 wks	Plasma folate	Immunoassay (Abbott IMX)	**Baseline:** 250 µg FA/d (n=22)	14.6 ± 4.7[5]	Unavailable	Unavailable
						Intervention: 4wks 250 µg FA/d (n=22)	20.4 ± 4.1[5]	Unavailable	Unavailable

Brouwer, I. 1999 [15]	Randomized controlled trial	144 healthy women Age:18-40[7] Netherlands	250 µg FA/d or 500 µg FA/d for 4wks	Plasma folate	Immunoassay (Abbott IMX)	**Baseline:** 250 µg FA (n=45) 500 µg FA (n=50) **Intervention: 4 wks** 250 µg FA (n=45) 500 µg FA (n=50)	 11 ± 3.4[5] 11 ± 4.0[5] 23 ± 5.3[5] 27 ± 5.1[5]	 Unavailable Unavailable	 Unavailable Unavailable
Brouwer, I. 2000 [16]	Dietary intervention trial	22 women (18-40y) Nijmegen, Netherlands	500 µg FA/2d or 250 µg FA/d for 4 wks	Plasma folate	Immunoassay (Abbott IMX)	**Baseline:** 500 µg FA/2d (n=11) 250 µg FA/d (n=11) **Intervention: 4wks** 500 µg FA/2d (n=11) 250 µg FA/d (n=11)	 Unavailable 9.1 (1.9, 16.3)[12] 11.4 (6.8, 15.9)[12]	 Unavailable Unavailable	 Unavailable Unavailable
Carlsson, CM. 2004 [17]	Prospective, single-blinded study	27 males and females Age: 70-88[7]	After 10wk placebo all treated with 400 µg FA/d for 10 wks, then a placebo washout for 10 wks, then 1400 µg FA/d for 10 weeks	Serum folate	Chemiluminescent enzymatic immunoassay	**Baseline** 400 µg/d (n=20) 1400 µg/d (n=17) **Intervention: 10 weeks** 400 µg/d (n=20) 1400 µg/d (n=17)	 24.1 ± 1.4[6,9] 27.0 ± 1.6[6,9] 37.7 ± 1.6[6,9] 43.1 ± 1.4[6,9]	 Unavailable Unavailable	 Unavailable Unavailable
Cheong, M. 2016 [18]	Double-blind, placebo-controlled trial	70 non-pregnant women Age: 21-35[7] Singapore	fortified milk powder with 400 µg FA/d for 12 weeks or placebo	Plasma and RBC folate	Microbiologic - *L. casei*	**Baseline:** 400 µg FA/d (n=29) **Intervention: 6 wks** 400 µg FA/d (n=29) **Intervention: 12 wks** 400 µg FA/d (n=29)	 28 ± 14[5] 71 ± 16[5] 82 ± 32[5]	 614 ± 186[5] 927 ± 242[5] 1200 ± 311[5]	 Unavailable Unavailable Unavailable
Cotlarciuc, I. 2011 [19]	Dietary intervention trial	101 healthy, female twins Age: 50-80[7] United Kingdom	0.8 mg FA/d for 6 wks	Plasma folate	Chemiluminescent, competitive immunoassay (Bayer Advia Centaur)	**Baseline:** MZ twins (n=51) DZ twins (n=50) **Intervention: 6 weeks** MZ twins (n=51) DZ twins (n=41)	 17.3 ± 6.6[5,9] 23.6 ± 11.7[5,9] 46.5 ± 10.7[5,9] 49.3 ± 8.9[5,9]	 Unavailable Unavailable	 Unavailable Unavailable
Cuskelly, GJ. 1996 [20]	Randomized, placebo-controlled trial	62 non-pregnant women Age: 17-40[7] United Kingdom	400 µg FA/d for 3 mo	RBC folate	Microbiologic - *L. casei*	**Baseline:** Supplement: 400 µg FA/d (n=9) Fortified food: 400 µg FA/d (n=6) **Intervention: 3mo** Supplement: 400 µg FA/d (n=9) Fortified food: 400 µg FA/d (n=6)	 Unavailable Unavailable	 796.8 ± 136.2[5,9] 740.0 ± 104.4[5,9] 1116.8 ± 267.9[5,9] 1130.5 ± 306.5[5,9]	 209 ± 37[5] 186 ± 35[5] 601 ± 43[5] 407 ± 76[5]

Daly, S. 2002 [21]	Double-blind, randomized placebo-controlled trial	Women of childbearing age (n=95) Dublin, Ireland	0, 100, 200 or 400 µg FA/d for 10 wks	RBC	Microbiologic - *L. casei*	**Baseline:** 100 µg FA/d (n=22) 200 µg FA/d (n=28) 400 µg FA/d (n=26) **Intervention: 10 wks** 100 µg FA/d (n=20) 200 µg FA/d (n=26) 400 µg FA/d (n=25)	Unavailable Unavailable	754.5 ± 199.0[5,9] 716.6 ± 160.9[5,9] 812.0 ± 243.2[5,9] 71.2 (-168.2, 205.4)[9,13] 263.3 (57.0, 452.6)[9,13] 273.0 (106.0, 545.7)[9,13]	Unavailable
Davis, BA. 1995 [22]	Placebo-controlled trial	20 non-pregnant women Age: 12-36[7] Northwestern South Carolina, USA	2000 µg FA/d for 4 wks	Serum and RBC folate	Microbiologic - *L. casei*	**Basline:** 2000 µg FA/d (n=10) **Intervention: 4 wks** 2000 µg FA/d (n=10)	7.8 ± 5.6[5] 29.4 ± 8.8[5]	469 ± 105[5] 549 ± 144[5]	Unavailable Unavailable
Deshmukh, U. 2010 [23]	Cluster randomized, placebo-controlled, double-blind, 2x3 factorial trial	119 families; 294 individuals (106 children, 92 fathers, 96 mothers) Age: Children: 9.0 ± 0.2[5] Fathers: 36.8 ± 3.7[5] Mothers: 30.4 ±3.1[5] 6 rural villages near Pune City, India	0 µg of vitamin B12 and 200 µg FA/d, 2 µg of vitamin B12 and 200 µg FA/d, or 10 µg of vitamin B12 and 200 µg of FA/d	Plasma folate	Microbiologic - *L. casei*	**Baseline:** 200 µg FA/d (n=151) **Intervention: 4 mo** 200 µg FA/d (n=151) **Intervention: 12 mo** 200 µg FA/d (n=151)	13.5 ± 5.6[5] 33.1 ± 16.1[5] 27.8 ± 14.4[5]	Unavailable Unavailable Unavailable	Unavailable Unavailable Unavailable
Dierkes, J. 1998 [24]	Randomized trial	36 healthy young women Age 24.7± 3.2[5] Germany	400 µg FA/d for 4 wks	Plasma folate	Protein binding test kit, Magic Lite (Ciba Corning Diagnostics GmbH, Fernwald, Germany)	**Baseline:** 400 µg FA/d (n=36) **Intervention: 4 wks** 400 µg FA/d (n=36)	17.8 (5.9, 31.5)[14] 32.9 (15.2, 67.0)[14]	Unavailable Unavailable	Unavailable Unavailable

Doshi, S. 2003 [25]	Double-blind, randomized, cross-over, controlled trial	50 subjects with CHD Age: 57± 8[5] United Kingdom	5000 µg FA/d for 6 wks	Plasma folate	competing protein binding assay kit	**Baseline:** 5000 µg FA/d (n=50)	20.2 ± 7.9[5,9]	Unavailable	Unavailable
						Intervention: 6 wks 5000 µg FA/d (n=50)	703.7 ± 533.5[5,9]	Unavailable	Unavailable
Doshi, SN. 2002 [26]	Randomized, placebo-controlled trial	33 patients Age: 55± 7[5] United Kingdom	5000 µg FA/d for 6 wks	Plasma folate	Competitive binding assay (Abbott IMX)	**Baseline:** 5000 µg FA/d (n=16)	22.37 ± 8.7[5]	Unavailable	Unavailable
						Intervention: 6 wks 5000 µg FA/d (n=16)	604.22 ± 429[5]	Unavailable	Unavailable
Dragani 2010 [27]	Dietary intervention trial	41 subjects Age: 42±12[5] Italy	5000 µg FA/d for 8 wks	Serum folate	Radioimmunoassay (ICN, New York, USA)	**Baseline:** 5000 µg FA/d (n=23 hyperhomocysteinaemic T allele carriers) 5000 µg FA/d (n=18 MTHFR CC controls)	10.0 ± 5.7[5] 15.0 ± 7.9[5]	Unavailable	Unavailable
						Intervention: 8 wks 5000 µg FA/d (n=23 hyperhomocysteinaemic T allele carriers) 5000 µg FA/d (n=18 MTHFR CC controls)	45.5 ± 31.6[5] 41.1 ± 18.8[5]	Unavailable	Unavailable
Durga, J. 2007 [28]	Randomized controlled trial	728 men and women Age: 50-70[7] Netherlands	800 µg FA/d for 3 years	RBC and Serum folate	Chemiluminescent immunoassay (Immulite 2000; Diagnostic Products Company, California, USA)	**Baseline:** 800 µg/d FA (n=355)	11.5 (9.4, 14.6)[8]	n/a[10]	195 (159, 241)[8]
						Intervention: 1 year 800 µg/d FA (n=347)	52.7 (43.2, 85.8)[8]	n/a[10]	Unavailable
						Intervention: 2 years 800 µg/d FA (n=340)	49.4 (41.7, 81.5)[8]	n/a[10]	Unavailable
						Intervention: 3 years 800 µg/d FA (n=344)	75.0 (50.0, 102.8)[8]	n/a[10]	181 (152, 219)[8]
Duthie, S. 2010 [29]	Double-blind, randomized controlled trial	20 participants Age: 39.9± 3.5[5]	1200 µg FA/d for 12 wks	Plasma folate	Chemiluminescence immunoassay (Abbott IMX)	**Baseline:** 1200 µg FA (n=10)	15.11 ± 1.58[6]	Unavailable	Unavailable
						Intervention: 12wks 1200 µg FA (n=10)	92.49 ± 11.71[6]	Unavailable	Unavailable
Earnest, C. 2002 [30]	Dietary intervention trial	150 men and women Age: 24-79[7] Texas, USA	800 µg FA/d for 24 weeks	Plasma folate	Microbiologic - *L. casei*	**Baseline:** 800 µg FA/d (n=141)	21.07 ± 7.7[5]	Unavailable	Unavailable
						Intervention: 12 wks 800 µg FA/d (n=141)	29.68 ± 8.6[5]	Unavailable	Unavailable
						Intervention: 24 wks 800 µg FA/d (n=141)	28.10 ± 9.1[5]	Unavailable	Unavailable
Ebisch, IMW. 2006 [31]	Randomized, controlled trial	87 males Age: 30-40[7] Netherlands	5000 µg FA/d and 6600 µg zinc sulphate for 26 wks	Serum folate	Radioassay (Dualcount Solid Phase Boil radioassay, Diagnostic Products Corp., California, USA)	**Baseline:** 5000 µg FA/d +zinc (n=18, subfertile male) 5000 µg FA/d +zinc (n=24, fertile male)	18.0 (13.0, 22.8)[8] 18.0 (15.0, 21.0)[8]	Unavailable	Unavailable

						Intervention: 26 wks 5000 µg FA/d +zinc (n=18, subfertile male) 5000 µg FA/d +zinc (n=24, fertile male)	105.0 (86.5, 122.5)[8] 110.0 (77.0, 130.0)[8]	Unavailable	Unavailable
Fohr, I. 2002 [32]	Randomized control trial	160 healthy, nonpregnant females Age: 19-39[7] Germany	400 µg FA/d for 8 wks	RBC and Plasma folate	Immunoassay (Abbott IMX) for Plasma folate; Microbiologic - *L. casei* for RBC folate	**Baseline:** FA group: 400 µg FA/d (n=51)	15.0 ± 4.9 (14.3)[15]	372 ± 132 (354)[15]	Unavailable
						Intervention: 4 wks FA group: 400 µg FA/d (n=51)	24.3 ± 5.8 (23.5)[15]	Unavailable	Unavailable
						Intervention: 8 wks FA group: 400 µg FA/d (n=51)	27.9 ± 8.0 (26.6)[15]	608 ± 112 (598)[15]	Unavailable
Gamble, M. 2006 [33]	Randomized control trial	194 males, females Age: 18-65[7] Rural region in Bangladesh	400 µg FA/d for 12 wks	Plasma folate	Radioimmunoassay (Quantaphase II; Bio-Rad Laboratories, California, USA)	**Baseline:** Folate group: 400 µg FA/d (n=96)	8.28 ± 4.74[5]	Unavailable	Unavailable
						Intervention: 12 wks Folate group: 400 µg FA/d (n=96)	61.57 ± 27.67[5]	Unavailable	Unavailable
Green, T. 2004 [34]	Randomized control trial	73 females Age: 18-45[7] Dunedin, New Zealand	400 µg FA/d through fortified milk for 6 wks	RBC and Plasma folate	Microbiologic - *L. casei*	**Baseline:** 375 µg FA Fortified milk/d (n=36)	21 (18, 23)[16]	834 (754, 913)[16]	Unavailable
						Intervention: 6 wks 375 µg FA Fortified milk/d (n=36)	48 (42, 53)[16]	1023 (955, 1091)[16]	889 (862, 915)[16]
						Intervention: 12 wks 375 µg FA Fortified milk/d (n=36)	51 (46, 56)[16]	1245 (1154, 1335)[16]	Unavailable
Green, T. 2013 [35]	Double-blind, randomized controlled trial	30 healthy men/women Age: 18-45[7] Vancouver, Canada	Daily consumption of wheat roll that contains 400µg folic acid for 16 wks	Plasma folate and whole blood folate	Microbiologic - *L. casei*	**Baseline:** 400 µg FA (n=14)	40 ± 12[5]	780 ± 190[5]	Unavailable
						Intervention: 8wks 400 µg FA (n=14)	56 ± 17[5]	1180 ± 310[5]	Unavailable
						Intervention: 16 wks 400 µg FA (n=14)	59 ± 19[5]	1160 ± 390[5]	Unavailable
Green, TJ. 2003 [36]	Dietary intervention trial	78 Women Age:18-49[7] New Zealand	400 µg/d FA for 12 weeks or placebo	RBC folate	Microbiologic - *L. casei*	**Baseline:** 400 µg/d FA (n=35)	Unavailable	650 ± 216[5]	224 ± 71[5]
						Intervention: 12 weeks 400 µg/d FA (n=35)	Unavailable	1104 ± 305[5]	Unavailable
Grieger, J. 2009 [37]	Dietary intervention trial	107 elderly participants Age: 79.9± 10.1[5] Victoria, Australia	Daily consumption of fortified milk for 6mo - mean of 120 µg FA/d	Serum folate	Radioimmunoassay (BioRad Laboratories, New South Wales, Australia)	**Baseline:** 120 µg FA/d (n=107)	13.4 ± 19.7[5]	Unavailable	Unavailable
						Intervention: 24 wks 120 µg FA/d (n=107)	17.9 ± 18.1[5]	Unavailable	Unavailable

Haglund, O. 1993 [38]	Double-blind, cross-over, dietary intervention trial	12 healthy men Mean age: 48	10 mg FA/d for 4 wks	Serum folate	Radioassay (SimulTRACK, Becton Dickinson, New York, USA)	**Baseline:** 10000 µg FA/d (n=12)	16.5 ± 10.1[5]	Unavailable	Unavailable
						Intervention: 4wks 10000 µg FA/d (n=12)	53.3 ± 2.3[5]	Unavailable	Unavailable
Hao, L. 2008 [39]	Randomized control trial	1108 females Age: 24-42[7] Hebei Province, China	100 µg FA/d, 400 µg FA/d, 4000 µg FA/d, or 4000 µg FA/wk for 6 mo	RBC and Plasma folate	Microbiologic - *L. casei*	**Baseline:** 100 µg FA/d (n=339)	9.7 (9.2, 10.2)[17]	594.7 (572.4, 617.8)[17]	Unavailable
						400 µg FA/d (n=338)	9.6 (9.1, 10.2)[17]	603.1 (580.5, 626.6)[17]	
						4000 µg FA/d (n=167)	9.7 (9.0, 10.5)[17]	599.4 (567.7, 632.9)[17]	
						4000 µg FA/wk (n=157)	9.8 (9.0, 10.6)[17]	610.8 (577.5, 646.1)[17]	
						Intervention: 1 mo 100 µg FA/d (n=339)	18.0 (17.0, 19.0)[17]	630.7 (607.1, 655.3)[17]	Unavailable
						400 µg FA/d (n=338)	29.8 (28.3, 31.5)[17]	728.7 (701.4, 757.1)[17]	
						4000 µg FA/d (n=167)	55.1 (51.0, 59.6)[17]	866.1 (820.2, 914.5)[17]	
						4000 µg FA/wk (n=157)	20.9 (19.3, 22.7)[17]	638.4 (603.6, 675.2)[17]	
						Intervention: 3 mo 100 µg FA/d (n=339)	19.0 (18.0, 20.1)[17]	659.2 (634.5, 684.8)[17]	Unavailable
						400 µg FA/d (n=338)	36.5 (34.5, 38.5)[17]	914.7 (879.8, 949.7)[17]	
						4000 µg FA/d (n=167)	68.9 (63.8, 74.5)[17]	1342.2 (1271.2, 1417.2)[17]	
						4000 µg FA/wk (n=157)	23.9 (22.0, 25.9)[17]	781.8 (739.2, 827.0)[17]	
						Intervention: 6 mo 100 µg FA/d (n=339)	20.2 (19.1, 21.3)[17]	759.5 (731.1, 789.1)[17]	Unavailable
						400 µg FA/d (n=338)	34.5 (32.7, 36.5)[17]	1035.5 (996.6,	

								1075.8)[17]	
						4000 µg FA/d (n=167)	54.3 (50.3, 58.7)[17]	1419.8 (1344.6, 1499.1)[17]	
						4000 µg FA/wk (n=157)	23.7 (21.8, 25.6)[17]	888.6 (840.1, 939.9)[17]	
Herrmann, M. 2006 [40]	Ranomized controlled trial	61 healthy males and females Age: 58.5 ± 8[5]	Daily 0.4, 1 or 5 mg FA for 2 months	Serum folate	Chemiluminescent immunassay (Bayer Healthcare, Ferwald, Germany)	**Baseline:** 0.4 mg FA/d (n=18) 1 mg FA/d (n=15) 5 mg FA/d (n=17)	 12.49 ± 5.45[5,9] 11.12 ± 2.95[5,9] 14.30 ± 10.44[5,9]	Unavailable	Unavailable
						Intervention: 4 weeks 0.4 mg FA/d (n=18) 1 mg FA/d (n=15) 5 mg FA/d (n=17)	 32.47[18,9] 29.13[18,9] 76.65[18,9]	Unavailable	Unavailable
						Intervention: 8 weeks 0.4 mg FA/d (n=18) 1 mg FA/d (n=15) 5 mg FA/d (n=17)	 50.58[18,9] 48.93[18,9] 45.19[18,9]	Unavailable	Unavailable
Heseker, H. 1987 [41]	Dietary intervention trial	6 healthy subjects Age: 26-43[7] Germany	1000 µg FA/d for 17 wks	Plasma folate	Radioassay (Becton Dickinson)	**Baseline:** 1000 µg FA/d (n=6)	12.49[9,18]	Unavailable	Unavailable
						Intervention: 4wks 1000 µg FA/d (n=6)	24.52[9,18]	Unavailable	Unavailable
						Intervention: 15wks 1000 µg FA/d (n=6)	29.06[9,18]	Unavailable	Unavailable
						Intervention: 17 wks 1000 µg FA/d (n=6)	29.51[9,18]	Unavailable	Unavailable
Heseker, H. 1993 [42]	Double-blind, randomized, placebo-controlled trial	498 men Age: 17-29[7]	800 µg F/d for 8 wks	Plasma folate	Radioassay (Clinical Assays)	**Baseline:** 800 µg F/d (n=498)	15.80 (0.24)[6]	Unavailable	Unavailable
						Intervention: 8 wks 800 µg F/d (n=498)	34.00 (0.62)[6]	Unavailable	Unavailable
Hiraoka, M. 2004 [43]	Dietary intervention trial	250 healthy, nonpregnant females Age: 19-29[7] Japan	2 wk baseline period was followed by two 4 wk treatment periods (200 and 400 µg/d FA supplementation) with a 4 wk washout period in between	Serum folate	Chemiluminescence immunoassay (ACS Folate II, ADVIA Centaur, Bayer Medical)	**Baseline:** Young women (n=100)	19.64 ± 10.21[5]	Unavailable	316.37 ± 100.95[5]
						Intervention: 6 wks 200 µg/d (n=100)	27.51 ± 13.1[5]	Unavailable	318.08 ± 137.71[5]
						Intervention: 14 wks 400 µg/d (n=100)	34.0 ±8.64[5]	Unavailable	311.94 ± 136.69[5]
Holmes, T. 2003 [44]	Randomized controlled trial	41 Caucasian men Age: >58 Oklahoma, USA October 1999-June 2000	fortified cereals containing 400 µg per serving per day	Serum folate	Radioimmunoassay (Cobra II, Auto-Gamma Counter; Packard Instrument Co.)	**Baseline:** 400 µg FA (n=21)	22.7 ± 6.8[5,9]	Unavailable	Unavailable

						Intervention: 4wks 400 µg FA (n=21)	29.5 ± 6.8[5,9]	Unavailable	Unavailable
						Intervention: 8wks 400 µg FA (n=21)	29.5 ± 4.5[5,9]	Unavailable	Unavailable
						Intervention: 20 wks 400 µg FA (n=21)	34.1 ± 6.8[5,9]	Unavailable	Unavailable
Hursthouse, N. 2011 [45]	Randomized control trial	119 healthy females Age: 18-40[7] New Zealand Aµgust 2008 - May 2009	140 µg FA/d or 400 µg FA/d for 40 wks	RBC and Plasma folate	Microbiologic Assay- *L. rhamnosus* (ATCC 27773; American Type Culture Collection, Manassas, VA)	**Baseline:** 140 µg FA/d: (n=49)	19.5 (16.5, 22.5)[17]	711.8 (626.1, 797.5)[17]	248.0 ± 1.6[19]
						400 µg FA/d: (n=48)	19.2 (16.3, 22.2)[17]	755.5 (664.2, 846.8)[17]	271.5 ± 1.5[19]
						Intervention: 6 wks 140 µg FA/d: (n=47)	26.6 (22.5, 30.8)[17]	834.5 (732.8, 936.1)[17]	Unavailable
						400 µg FA/d: (n=42)	37.3 (31.2, 43.3)[17]	910.8 (796.2, 1025.3)[17]	
						Intervention: 12 wks 140 µg FA/d: (n=44)	28.0 (23.6, 32.5)[17]	849.0 (743.4, 954.7)[17]	Unavailable
						400 µg FA/d: (n=41)	38.3 (32.1, 44.6)[17]	940.1 (821.2, 1059.1)[17]	
						Intervention: 29 wks 140 µg FA/d: (n=41)	31.0 (25.9, 36.0)[17]	987.0 (861.8, 1112.2)[17]	Unavailable
						400 µg FA/d: (n=40)	37.3 (31.1, 43.4)[17]	1121.7 (977.9, 1265.4)[17]	
						Intervention: 40 wks 140 µg FA/d: (n=42)	29.0 (24.3, 33.7)[17]	1111.3 (970.3, 1252.3)[17]	Unavailable
						400 µg FA/d: (n=39)	39.5 (33.0, 46.1)[17]	1273.4 (1110.2, 1436.6)[17]	
Johansson, M. 2002 [46]	Dietary intervention trial	29 healthy women Age: 23-50[7] Sweden January 2001	Wheat breakfast rolls that contained 166 µg FA. One roll eaten per day	Serum folate	Protein binding (Abbott IMX)	**Baseline:** 166 µg FA (n=14)	16.9 ± 4.3[5]	Unavailable	Unavailable
						Intervention: 4 wks 166 µg FA (n=14)	21.2 ± 2.4[5]	Unavailable	Unavailable

						Intervention: 8 wks 166 µg FA (n=14)	22.4 ± 1.3[5]	Unavailable	Unavailable
						Intervention: 12 wks 166 µg FA (n=14)	22.0 ± 2.1[5]	Unavailable	Unavailable
Kauwell, G. 2000 [47]	Dietary intervention trial	33 healthy women Age: 60-85[7] Florida, USA	7 weeks of 82 or 301 µg FA/d throµgh folate restricted diet and FA throµgh apple juice.	Serum folate	Microbiologic - *L. casei*	**Baseline:** 82 µg FA (n=8) 301 µg FA (n=7)	10.8 ± 4.4[5] 15.8 ± 6.9[5]	Unavailable	Unavailable
						Intervention: 7 wks 82 µg FA (n=7) 301 µg FA (n=8)	16.2 ± 10.0[5] 32.0 ± 10.6[5]	Unavailable	Unavailable
Klerk, M. 2004 [48]	Randomized control trial	276 males and females Age: 50-70[7] Sept - Dec 2000	0.8 mg FA/d for 1 year	Serum folate	Chemiluminescent immunoassay analyzer (Immulite 2000; Diagnostic Products Company, Los Angeles)	**Baseline:** 0.8 mg/d FA (n=137)	12.4 (10.2, 15.6)[8]	Unavailable	Unavailable
						Intervention: 1 yr 0.8 mg/d FA (n=137)	49.5 (42.3, 90.3)[8]	Unavailable	Unavailable
Kok, DEG. 2015 [49]	Double-blind, randomized, placbo-controlled trial	92 participants Age: 65-75[7] Netherlands	400 µg FA/d or placebo for 2 years	Serum folate	Electro-chemiluminescence immunoassay (Elecsys 2010, Roche, Almere, Netherlands)	**Baseline:** 400 µg FA/d (n=44)	16.2 (13.1, 24.4)[8]	Unavailable	Unavailable
						Intervention: 2 years 400 µg FA/d (n=44)	52.3 (45.1, 67.6)[8]	Unavailable	Unavailable
Lamers, Y. 2004 [50]	Controlled trial	34 female Age: 18 – 25[7] Bonn, Germany Jan - July 2002	**Intervention:** FA and MTHF supplement feeding study (24wk) Dietary intake using 3-d diet records at baseline, weeks 8, 16, 24	Plasma folate	Immunoassay (AxSYM Analyzer, Abbott Laboratories)	**Baseline** 400 µg FA/d (n=34)	14.4 (12.6, 16.5)[17]	Unavailable	Unavailable
						Intervention: 4 wks 400 µg FA/d (n=34)	28.8 (26.3, 31.5)[17]	Unavailable	Unavailable
						Intervention: 8 wks 400 µg FA/d (n=34)	34.9 (32.6, 37.4)[17]	Unavailable	Unavailable
						Intervention: 12 wks 400 µg FA/d (n=34)	35.7 (33.4, 38.0)[17]	Unavailable	Unavailable
						Intervention: 16 wks 400 µg FA/d (n=34)	37.1 (34.4, 40.0)[17]	Unavailable	Unavailable
						Intervention: 20 wks 400 µg FA/d (n=34)	37.6 (35.5, 39.9)[17]	Unavailable	Unavailable
						Intervention: 24 wks 400 µg FA/d (n=34)	34.7 (32.6, 37.0)[17]	Unavailable	Unavailable
Liem, A. 2003 [51]	Randomized controlled trial	593 cardiology patients, Age: 64.9± 9.9[5]	500 µg FA/d for 36 months	Serum folate	Ion capture (Abbott IMX)	**Baseline:** 500 µg FA/d (n=300)	17 ± 7[5]	Unavailable	Unavailable
						Intervention: 12 wks 500 µg FA/d (n=300)	33 ± 6[5]	Unavailable	Unavailable
Lin, P. 2006 [52]	Randomized, placebo-controlled trial	46 cardiology patients Age: 74.6 ±7.8[5] Taiwan	240 µg FA/d for 8 wks	Serum folate	Chemiluminescent Immunoassay	**Baseline:** 240 µg FA/d (n=24)	22.2 ± 10.9[5]	Unavailable	Unavailable

						Intervention: 4 wks 240 µg FA/d (n=24)	36.3 ± 18.4[5]	Unavailable	Unavailable
						Intervention: 8 wks 240 µg FA/d (n=24)	41.7 ± 16.8[5]	Unavailable	Unavailable
Mann, BA. 1987 [53]	Randomized, double-blind, placebo-controlled trial	101 elderly men/women, Age: 59-81[7] New Mexico, USA	400 µg FA/d for 16 weeks	Plasma folate	Radioassay (Becton Dickinson Immunodiagnostics, New York, USA)	**Baseline:** 400 µg FA/d (n=25) men 400 µg FA/d (n=28) women	19.1 ± 7.9[5,9] 17.3 ± 5.7[5,9]	Unavailable	Unavailable
						Intervention: 8 wks 400 µg FA/d (n=25) men 400 µg FA/d (n=28) women	33.1 ± 13.2[5,9] 28.6 ± 7.3[5,9]	Unavailable	Unavailable
						Intervention: 16 wks 400 µg FA/d (n=25) men 400 µg FA/d (n=28) women	32.5 ± 5.4[5,9] 37.9 ± 10.0[5,9]	Unavailable	Unavailable
Mao, G. 2008 [54]	Double-blind, randomized controlled trial	480 patients with mild-moderate primary hypertension Age: 27-75[7] China	10 mg of enalapril + 400µg FA/d, 10 mg of enalapril + 800 µg FA/d, or placebo for 8wks	Serum folate	Chemiluminescent immunoassay (Beckman-Coulter Canada, Inc., Mississaµga, Canada)	**Baseline:** 400 µg FA/d + enalapril (n=146) 800 µg FA/d + enalapril (n=148)	12.6 ± 1.5[19] 12.5 ± 1.5[19]	Unavailable	Unavailable
						Intervention: 8wks 400 µg FA/d + enalapril (n=146) 800 µg FA/d + enalapril (n=148)	23.7 (1.5)[19] 26.7 (1.5)[19]	Unavailable	Unavailable
Martin-Bautista, E. 2010 [55]	Double-blind, randomized controlled trial	72 participants Age: 30-65[7] Granada, Spain	150 µg FA/d throµgh enriched milk or control milk for 1 yr	Serum folate	Radioimmunoassay (SimulTrac-SNB radioassay; MP Biomedicals, Ohio, USA)	**Baseline:** 150 µg FA/d (n=39)	47.7 ± 4.9[6,9]	Unavailable	Unavailable
						Intervention: 12 wks 150 µg FA/d (n=39)	66.9 ± 4.4[6,9]	Unavailable	Unavailable
						Intervention: 24 wks 150 µg FA/d (n=39)	86.5 ± 6.3[6,9]	Unavailable	Unavailable
						Intervention: 48 wks 150 µg FA/d (n=39)	72.9 ± 4.5[6,9]	Unavailable	Unavailable
McKay, DL. 2000 [56]	Randomized, double-blind, placebo-controlled trial	80 free living men and women Age: 50-70[7] Boston, MA, USA	400 µg FA/d for 8 wks or placebo	Plasma folate	Radioimmunoassay (Quantaphase II; BioRad Laboratories, California, USA)	**Baseline:** 400 µg FA/d (n=41)	23.3 ± 7.5[5]	Unavailable	378 ± 209[5]
						Intervention: 8 wks 400 µg FA/d (n=41)	33.0 ± 8.4[5]	Unavailable	Unavailable
Meer, K. 2005 [57]	Double-blind, randomized controlled trial	12 healthy volunteers Age: 18-30 years or older than 50 years Amsterdam	400 µg FA/d for 5 wks	Serum folate	Chemiluminescent immunoassay (Chiron Diagnostics, Halstead, UK)	**Baseline:** 400 µg FA (<30y, n=6) 400 µg FA (>50y, n=6)	13.3 (8.9-23.1)[11] 16.7 (6.4-20.7)[11]	Unavailable	Unavailable
						Intervention: 5wks 400 µg FA (<30y, n=6) 400 µg FA (>50y, n=6)	22.1 (10.1-30.0)[11] 23.7 (18.3-30.5)[11]	Unavailable	Unavailable

Melse-Boonstra, A. 2004 [58]	Randomized control trial	180 males, females Age: 50-75[7] Netherlands	145 µg of hepatoglutamyl FA/d or 320 µg of monoglutamyl FA/d for 12 wks	RBC and Serum folate	Chemiluminescent immunoassay (Immulite 2000; Diagnostic Products Company, Los Angeles)	**Baseline:** 323 nmol hepatoglutamyl FA/d (145 µg): (n=60) 262 nmol monoglutamyl FA/d (320 µg): (n=59)	 14.4 ± 5.4[5] 15.2 ± 4.1[5]	 n/a[10]	Unavailable
						Intervention: Week 2 323 nmol hepatoglutamyl FA/d (145 µg): (n=60) 262 nmol monoglutamyl FA/d (320 µg): (n=58)	 15.8 ± 4.6[5] 18.8 ± 4.7[5]	 n/a[10]	Unavailable
						Intervention: Week 12 323 nmol hepatoglutamyl FA/d (145 µg): (n=60) 262 nmol monoglutamyl FA/d (320 µg): (n=59)	 19.3 ± 5.6[5] 25.7 ± 7.4[5]	 n/a[10]	Unavailable
Nguyen, P. 2008 [59]	Randomized control trial	459 females Age: 15-49[7] Guatemala	12 wks of the following intake: Groups - 1: 5000 µg FA, 120 mg Fe, 30 mg Zn, 16.8 µg B12 WEEKLY 2: 2800 µg FA, 120 mg Fe, 0 mg Zn, 16.8 µg B12 WEEKLY 3: 400 µg FA, 60 mg Fe, 15 mg Zn, 2.4 µg B12 DAILY 4: 200 µg FA, 60 mg Fe, 0 mg Zn, 2.4 µg B12 DAILY	Serum folate	Microbiologic - *L. casei*	**Baseline:** Group 1: 5000 µg weekly (n=87) Group 2: 2800 µg weekly (n=91) Group 3: 400 µg daily (n=80) Group 4: 200 µg daily (n=96)	 31.0 (28.4, 33.6)[20] 31.8 (29.3, 34.3)[20] 33.1 (30.4, 35.7)[20] 31.1 (28.7, 33.6)[20]	Unavailable	384 (292-524)[8] 370 (252-485)[8] 340 (246-540)[8] 364 (281-483)[8]
						Intervention: 12 wks Group 1: 5000 µg weekly (n=86) Group 2: 2800 µg weekly (n=90) Group 3: 400 µg daily (n=79) Group 4: 200 µg daily (n=96)	 46.2 (44.1, 48.4)[20] 46.2 (44.1, 48.3)[20] 47.9 (45.7, 50.2)[20] 48.1 (46.1, 50.1)[20]	Unavailable	Unavailable
Nguyen, P. 2009 [60]	Dietary intervention trial	40 nonpregnant, healthy females Age: 18-45[7] Toronto, ON, Canada March 2007 - February 2008	1.1 mg FA/d or 5 mg FA/d for 30 wks	RBC and Plasma folate	Microbiological assay with *Lactobacillus rhamnosus* (ATCC 7469; American Type Tissue Culture Collection, Manassas, VA)	**Baseline:** 1.1 mg FA/d (n=20) 5 mg FA/d (n=20)	 49.4 ± 15.7[5] 48.8 ± 14.5[5]	1035 ± 273[5] 1121 ± 410[5]	376 ± 128[5] 353 ± 129[5]
						Intervention: 30 wks 1.1 mg FA/d (n=19) 5 mg FA/d (n=19)	 96.8 ± 41.1[5] 165.3 ± 109.9[5]	1625 ± 339[5] 2339 ± 782[5]	357 ± 132[5] 380 ± 170[5]
Norsworthy, B. 2001 [61]	Randomized controlled trial	114 nonpregnant women Age: 18-40[7] Dunedin, New Zealand July 2000- October 2000	2800 µg FA/wk or 400 µg FA/d for 12 wks	Plasma folate and RBC	Microbiologic - *L. casei*	**Baseline:** 2800 µg FA/wk (n=37) 400 µg FA/d (n=35)	 20 (17, 24)[17] 18 (16, 21)[17]	608 (553, 668)[17]	Unavailable

								615 (560, 677)[17]	
						Intervention: 6 wks			
						2800 µg FA/wk (n=37)	28 (25, 32)[17]	747 (685, 816)[17]	Unavailable
						400 µg FA/d (n=35)	38 (32, 43)[17]	863 (797, 935)[17]	
						Intervention: 12 wks			
						2800 µg FA/wk (n=37)	32 (28, 36)[17]	900 (828, 978)[17]	Unavailable
						400 µg FA/d (n=35)	44 (39, 49)[17]	1053 (957, 1158)[17]	
Olthof, M. 2006 [62]	Randomized, double blind, crossover, control trial	40 healthy males and females Age: 50-70[7] Wageningen University in the Netherlands	0.8 mg FA/d for 6 wks	Serum folate	Chemiluminescent immunoassay (IMMULITE 2000)	**Baseline:**			
						0.8 mg FA/d (n=40)	16.8 ± 7.9[5]	Unavailable	Unavailable
						Intervention: 6 wks			
						0.8 mg FA/d (n=39)	53.0 ± 17.7[5]	Unavailable	Unavailable
Oort, F. 2003 [63]	Double-blind, randomized controlled trial	316 men and women Age: 50-75[7] Wageningen, Netherlands	50, 100, 200, 400, 600, 800 µg FA/d, or placebo for 12 wks	Serum folate	Chemiluminescent immunoassay (Immulite 2000, Diagnostic Products Company)	**Baseline:**			
						50 µg FA (n=42)	12.0 ± 3.1[5]	Unavailable	Unavailable
						100 µg FA (n=41)	12.7 ± 4.6[5]		
						200 µg FA (n=43)	12.3 ± 4.2[5]		
						400 µg FA (n=43)	13.8 ± 5.3[5]		
						600 µg FA (n=43)	12.9 ± 4.9[5]		
						800 µg FA (n=43)	12.9 ± 3.6[5]		
						Intervention: 4wks			
						50 µg FA (n=42)	14.7 ± 3.7[5]	Unavailable	Unavailable
						100 µg FA (n=41)	17.4 ± 6.2[5]		
						200 µg FA (n=43)	19.8 ± 5.7[5]		
						400 µg FA (n=43)	31.9 ± 15.3[5]		
						600 µg FA (n=43)	41.4 ± 19.4[5]		
						800 µg FA (n=43)	53.4 ± 28.3[5]		
						Intervention: 12 wks			
						50 µg FA (n=42)	16.3 ± 4.4[5]	Unavailable	Unavailable
						100 µg FA (n=41)	19.9 ± 7.6[5]		
						200 µg FA (n=43)	24.6 ± 7.5[5]		
						400 µg FA (n=43)	43.2 ± 21.0[5]		
						600 µg FA (n=43)	55.6 ± 24.5[5]		
						800 µg FA (n=43)	74.8 ± 43.3[5]		
Papandreou, D. 2010 [64]	Dietary intervention trial	524 children Age: 6-15[7] 8 public schools in Northern Greece	5 mg oral FA 2 times/wk	Serum folate	Immunoassay (Abbott IMX)	**Baseline:**			
						5mg oral FA 2x/wk (n=20)	9.8 (6.8 - 45.4)[9,21]	Unavailable	328 (170-627)[21]
						Intervention: 2 mo			
						5mg oral FA 2x/wk (n=20)	38.1 (15.9 - 45.4)[9,21]	Unavailable	388 (270-840)[21]

Pathansali, R. 2006 [65]	Randomized control trial	24 healthy, elderly males, females Age: ≥ 65	5 mg FA/d for 4 wks	Serum folate	Competitive protein binding immunoassays (Bayer Diagnostics, Newbury, Berkshire, UK)	**Baseline:** 5 mg/d FA: (n=12)	13.62 ± 5.22[5,9]	Unavailable	Unavailable
						Intervention: 4 wks 5 mg/d FA: (n=12)	45.17 ± 1.36[5,9]	Unavailable	Unavailable
Pena, A. 2007 [66]	Double-blind, randomized controlled trial	53 obese adolescents Age: 13.0 ± 2.18[5] Adelaide, Australia January 2004- January 2006	5000 µg FA/d or placebo for 8wks	Serum folate	Chemiluminescent microparticle folate-binding protein assay (Abbott Laboratories)	**Baseline:** 5000 µg FA/d (n=27)	18.60 ± 9.72[5]	Unavailable	Unavailable
						Intervention: 8 wks 5000 µg FA/d (n=27)		Unavailable	Unavailable
Petrogianni, M. 2012 [67]	Randomized control trial	101 Hypercholesterolaemic adults Age: 40-60[7] Athens, Greece	500 µg FA/d through consumption of enriched milk for 3 mo	Plasma folate	Electrochemiluminescence (Roche E170)	**Baseline:** 500 µg FA/d (n=40)	19.1 ± 7.5 [9,5]	Unavailable	Unavailable
						Intervention: 3 mo 500 µg FA/d (n=40)	32.9 ± 9.5 [9,5]	Unavailable	Unavailable
Pinto, X. 2005 [68]	Randomized, crossover, dietary intervention trial	20 male patients with history of coronary artery disease Age: 60.9± 8.91[5] Spain	500 µg FA/d for 5 wks or 370 µg food folate & 130 µg FA; followed by 5 wks washout then switch	Serum folate	Radioassay (SimulTRACK, Becton Dickinson, New York, USA)	**Baseline:** 500 µg FA/d (n=20) 370 µg food folate + 130 µg FA/d (n=20)	19.42 ± 7.53[5] 18.89 ± 6.46[5]	Unavailable	Unavailable
						Intervention: 5 wks 500 µg FA/d (n=20) 370 µg food folate + 130 µg FA/d (n=20)	34.53 ± 10.12[5] 27.55 ± 9.48[5]	Unavailable	Unavailable
Pullin, CH. 2001 [69]	Crossover, dietary intervention trial	Healthy subjects (n=126), 42 of each MTHFR genotype Age: 18-65[7] South Wales, United Kingdom	400 µg FA/d for 4 mo	Plasma folate	Abbott IMX methods	**Baseline:** CC (n=42) CT (n=42) TT (n=42)	19.1 ± 7.0[5,9] 17.7 ± 6.8[5,9] 14.8 ± 7.3[5,9]	Unavailable	254 ± 83[5]
						Intervention: 4 mo CC (n=35) CT (n=35) TT (n=36)	36.8 ± 25.2[5,9] 30.2 ± 8.4[5,9] 27.9 ± 8.6[5,9]	Unavailable	561 ± 98[5]
Qin, X. 2012 [70]	Randomized control trial	480 Chinese adults with mild or moderate hypertension Age: 18-75[7] Six hospitals in different Chinese regions (Ha'erbin, Shanghai, Shenyang, Beijing, Xi'an, and Nanjing) Sept - Dec 2005	Once per day Enalapril supplement with a) no FA b) with 0.4 mg FA c) with 0.8 mg FA (8 wks)	Serum folate	Chemiluminescent immunoassay (Beckman-Coulter Canada Inc., Mississaµga, Canada)	**Baseline:** Low-FA: Enalapril 10 mg combined with 0.4 mg FA /d (n=147) High-FA: Enalapril 10 mg combined with 0.8 mg FA /d (n=145)	13.7 ± 6.1[5] 13.5 ± 6.3[5]	Unavailable	Unavailable
						Intervention: 4 wks Low-FA: Enalapril 10 mg combined with 0.4 mg FA /d (n=147) High-FA: Enalapril 10 mg combined with 0.8 mg FA /d (n=145)	21.4 ± 9.2[5] 25.9 ± 11.0[5]	Unavailable	Unavailable

						Intervention: 8 wks Low-FA: Enalapril 10 mg combined with 0.4 mg FA /d (n=147) High-FA: Enalapril 10 mg combined with 0.8 mg FA /d (n=145)	24.1 ± 10.6[5] 26.9 ± 10.9[5]	Unavailable	Unavailable
Quinlivan, EP. 2002 [71]	Dietary intervention trial	30 healthy men with normal concentrations of folate and vitamin B12 Age: 34-65[7]	100 µg FA/d for 6 wks	Plasma folate	Microbiologic- *L. casei*	**Baseline:** Preintervention (n=30)	14.3 (11.4, 22.7)[8,9]	Unavailable	Unavailable
						Intervention: 6 wks 100 µg FA/d (n=30)	18.8 (15.0, 25.4)[8,9]	Unavailable	Unavailable
						Intervention: 12 wks 200 µg FA/d (n=30)	24.4 (19.7, 33.1)[8,9]	Unavailable	Unavailable
						Intervention: 26 wks 400 µg FA/d (n=30)	40.1 (29.7, 46.1)[8,9]	Unavailable	Unavailable
		23 healthy women with normal concentrations of folate and vit B12	500 µg FA/d for 4 mo			**Baseline:** 500 µg FA/d (n=23)	19.5 (10.0, 23.8)[8,9]	Unavailable	Unavailable
						Intervention: 4 mo 500 µg FA/d (n=23)	35.2 (21.1, 40.4)[8,9]	Unavailable	Unavailable
Raigani, M. 2014 [72]	Randomized, placebo-controlled trial	83 infertile men Iran	5000 µg FA and placebo, FA and zinc sulphate, or placebo and placebo for 16 wks	Serum folate	radioimmunoassay (MP Biomedicals Simul-TRAC-SNB, New York USA)	**Baseline:** 5000 µg FA/placebo (n=20) 5000 µg FA/Zinc sulphate (n=21)	9.1 (5.9, 17.3)[8,9] 9.5 (7.0, 14.8)[8,9]	Unavailable	Unavailable
						Intervention: 16 wks 5000 µg FA/placebo (n=20) 5000 µg FA/Zinc sulphate (n=21)	73.5 (33.8, 110.5)[8,9] 76.0 (27.3, 154.4)[8,9]	Unavailable	Unavailable
Rhode, BM. 1983 [73]	Dietary intervention trial	57 non pregnant women	60 µg FA/d for 7 wks	Serum folate	Microbiologic - *L. casei*	**Baseline:** 60 µg FA/d (n=20)	19.1 ± 1.6[6,9]	Unavailable	Unavailable
						Intervention: 7 wks 60 µg FA/d (n=20)	46.5 ± 13.2[6,9]	Unavailable	Unavailable
Rosenthal, J. 2008 [74]	Randomized, double-blind control trial	140 women Age:18-49[7] Choloma, Honduras	1 mg FA/d or 5mg FA/wk for 12 weeks	Serum folate and RBC folate	Radioassay	**Baseline:** 5 mg/week (n=58) 1 mg/d (n=50)	15.66 ± 0.68[6,9] 14.30 ± 0.45[6,9]	n/a[10]	Unavailable
						Intervention: 6 wks 5 mg/week (n=58) 1 mg/d (n=50)	19.75 ± 0.68[6,9] 27.69 ± 0.68[6,9]	n/a[10]	Unavailable
						Intervention: 12 wks 5 mg/week (n=58) 1 mg/d (n=50)	22.93 ± 0.91[6,9] 33.82 ± 1.36[6,9]	n/a[10]	Unavailable
Schorah, CJ. 1998 [75]	Randomized, double-blind, placebo-controlled trial	119 healthy volunteers aged 32-65 years Leeds, England	200 µg FA/d for 24 wks	Serum and RBC folate	Radioassay (Diagnostic Products Corporation)	**Baseline:** 200 µg FA/d (n=33) 200 µg FA/d + other vitamins (n=31)	19.7 (13.8, 23.2)[9,22] 17.5 (14.3, 20.7)[9,22]	n/a[10]	Unavailable
						Intervention: 4 wks 200 µg FA/d (n=33) 200 µg FA/d + other vitamins (n=31)	29.1 (22.2, 34.7)[9,22] 23.6 (18.4, 27.9)[22]	n/a[10]	Unavailable
						Intervention: 8 wks 200 µg FA/d (n=33) 200 µg FA/d + other vitamins (n=31)	26.1 (18.8, 25.2)[9,22] 24.1 (17.5, 28.6)[9,22]	n/a[10]	Unavailable

						Intervention: 24 wks 200 µg FA/d (n=33) 200 µg FA/d + other vitamins (n=31)	31.3 (20.9, 40.0)[9,22] 31.1 (20.7, 40.6)[9,22]	n/a[10]	Unavailable
Sharifi, F. 2010 [76]	Randomized, double-blind, placebo-controlled trial	42 hypertensive individuals, Age: 25-64[7] Tehran, Iran 2006	5000 µg FA/d for 6 weeks	Serum folate	Radioimmunoassay (SimulTrac, ICN Pharmaceuticals)	**Baseline:** 5000 µg FA/d (n=18)	16.1 ± 7.0[5,9]	Unavailable	Unavailable
						Intervention: 6 wks 5000 µg FA/d (n=18)	57.4 ± 7.0[5,9]	Unavailable	Unavailable
Sheu, W. 2005 [77]	Randomized control trial	74 obese females with BMI 29.6 ± 0.5 kgs/m2 Age: 41 ± 1[6] Taiwan	5 mg FA/d for 12 wks	Serum folate	Chemiluminescence kits within one run (IMMULITE, Diagnostic Products Corporation, Los Angeles, CA, USA)	**Baseline:** 5 mg FA/d: (n=36)	22.2 ± 1.5[6]	Unavailable	Unavailable
						Intervention: wk 12 5 mg FA/d: (n=36)	69.8 ± 10.1[6]	Unavailable	Unavailable
Shidfar, F. 2009 [78]	Randomized control trial	40 asymptomatic newly diagnosed hypercholesterolemic males and females Mean age: 44.87 ± 7.33[5] Tehran, Iran	5 mg FA/d for 8 wks	Plasma folate	Radioimmunoassay	**Baseline:** 5 mg/d (n=20)	5.08 ± 2.01[5]	Unavailable	Unavailable
						Intervention: 8 wks 5 mg/d (n=20)	14.29 ± 5.94[5]	Unavailable	Unavailable
Smidt, LJ. 1990 [79]	Double-blind, randomized, placebo-controlled trial	80 women Age: 65-92[7] Cork City, Ireland	400 µg FA/d for 6 wks	Plasma folate	Microbiologic - *L. casei*	**Baseline:** 400 µg FA/d (n=20) 400 µg FA/d + 10 µg thiamin (n=20)	13.6 ± 8.2[5] 9.1 ± 6.3[5]	Unavailable	Unavailable
						Intervention: 6wks 400 µg FA/d (n=20) 400 µg FA/d +10 µg thiamin (n=20)	43.0 ± 22.2[5] 40.8 ± 18.8[5]	Unavailable	Unavailable
Strandhagen, E. 2003 [80]	Randomized control Trial	121 healthy, nonsmoking males and females Age: 29-65[7] Gothenburg, Sweden	200 µg FA/d for 4 wks	Serum folate	Immunoassay (ADVIA Centaur)	**Baseline:** 200 µg FA/d (n=59)	11.9 ± 6.5[5]	Unavailable	Unavailable
						Intervention: week 4 200 µg FA/d (n=59)	20.8 ± 6.07[5]	Unavailable	Unavailable
Sweeney, M.R. 2007 [81]	Dietary intervention trial	20 healthy adult subjects (10 male, 10 female) Age: 20-40[7] Dublin, Ireland	400 µg FA/d for 14 wks	RBC and Serum folate	Microbiologic- *L. casei*	**Baseline:** 400 µg FA/d (n=19)	17.25 ± 9.65[5,9]	1084.99 ± 394.96[5,9]	Unavailable
						Intervention: 14 weeks 400 µg FA/d (n=19)	33.53 ± 11.37[5,9]	1575.24 ± 451.09[5,9]	Unavailable
Tapola, NS. 2004 [82]	Randomized, controlled, double-blinded, parallel trial	n=60 men and women Age: 48± 11[5] Eastern Finland	Mineral water fortified with 563 µg/d FA for 8 weeks or control	RBC and Serum folate	AutoDELFIA Folate time-resolved fluoroimmunoassay method (TR-FIA)	**Baseline:** 563 µg/d FA (n=31)	12.1 ± 4.4[5]	n/a[10]	324 ± 91[5]
						Intervention: 2 wks 563 µg/d FA (n=31)	20.0 ± 6.9[5]	n/a[10]	Unavailable

						Intervention: 4 wks 563 µg/d FA (n=31)	24.5 ± 7.6[5]	n/a[10]	875 ± 99[5]
						Intervention: 8 wks 563 µg/d FA (n=31)	28.2 ± 7.3[5]	n/a[10]	Unavailable
Tighe, T. 2011 [83]	Double-blind, randomized, placebo-controlled trial	172 patients Northern Ireland	placebo, 0.2, 0.4, 0.8 mg FA/day for 26 wks	Serum folate	Microbiologic - *L. casei*	**Baseline:** 2000 µg FA (n=44) 4000 µg FA (n=43) 8000 µg FA (n=45)	14.8 (14.1, 20.4)[9,17] 17.7 (16.6, 22.9)[9,17] 17.3 (16.6, 22.9)[9,17]	Unavailable	Unavailable
						Intervention: 26 wks 2000 µg FA (n=44) 4000 µg FA (n=43) 8000 µg FA (n=45)	32.9 (17.9, 28.4)[9,17] 53.6 (50.6, 64.2)[9,17] 77.0 (72.9, 86.7)[9,17]	Unavailable	Unavailable
Title, L. 2000 [84]	Double-blind, randomized controlled trial	50 participants Age:18-75[7] Novia Scotia, Canada	5 mg FA/d or 5 mg FA/d + 2g Vit C/d for 4 mo	Plasma folate	Immunoassay (Abbott IMX)	**Baseline:** 5000 µg FA (n=25) 5000 µg FA + 2g Vit C (n=25)	13.8 (11.8, 16.1)[17] 14.9 (13.3, 16.8)[17]	Unavailable	Unavailable
						Intervention: 4mo 5000 µg FA (n=25) 5000 µg FA + 2g Vit C (n=25)	79.2 (49.5, 126.7)[17] 80.1 (53.5, 119.9)[17]	Unavailable	Unavailable
Toprak, A. 2005 [85]	Randomized control trial	55 non-hysterectomized healthy postmenopausal females Istanbul, Turkey	Hormone therapy (HT) + 5 mg FA/d for 3 mo HT was 0.625 mg conjµgated equine estrogen, continuously combined with 2.5 mg medroxyprogesterone acetate daily	Serum folate	Electrochemiluminescence Immunoassay (Elecsys 2010, Roche Diagnostics)	**Baseline:** HT + 5 mg/d FA: (n=20)	21.57 ± 9.53[5,9]	Unavailable	Unavailable
						Intervention: 3 mos HT + 5 mg/d FA: (n=20)	40.41 ± 7.95[5,9]	Unavailable	Unavailable
Tsui, JC. 1990 [86]	Dietary intervention trial	23 adolescents Age: 12-15[7] Kansas City, Missouri, USA	400 µg FA/d for 8 wks	Serum folate	Radioassay	**Baseline:** 400 µg FA/d (n=23)	18.4 ± 8.1[6]	Unavailable	Unavailable
						Intervention: 8wks 400 µg FA/d (n=23)	29.2 ± 12.9[6]	Unavailable	Unavailable
Tucker, K. 2004 [87]	Randomized, double-blind trial	189 healthy, volunteers Age: 50-85[7]	Daily consumption of breakfast cereal fortified with 440 µg FA or placebo for 12 weeks	Plasma folate	Radioassay (Bio-Rad, California, USA)	**Baseline:** 440 µg/d FA (n=93)	24.7 ± 0.7[6]	Unavailable	375 ± 17[6]
						Intervention: 12 weeks 440 µg/d FA (n=93)	32.2 ± 0.7[6]	Unavailable	745 ± 14[6]
Ubbink, J. 1994 [88]	Randomized controlled trial	100 males with hyperhomocysteinemia (>16.3 µmol/L) Age: 20-73[7] Pretoria, South Africa	0.65 mg FA/d for 6 wks or 0.65 mg FA/d + 12.2 mg Pyridoxine + 0.4 mg Cobalamin for 6 wks	Plasma folate	Radioimmunoassay (Simul TRAC-SNB, Becton Dickinson, New York, USA)	**Baseline:** 0.65 mg FA/d: (n=19) Combo/d: 0.65 mg FA + 12.2 mg Pyridoxine + 0.4 mg Cobalamin (n=20)	6.0 ± 4.4[5] 5.2 ± 3.0[5]	Unavailable	Unavailable
						Intervention: 6 wks 0.65 mg FA/d: (n=19)	17.4 ± 10.4[5] 18.4 ± 11.1[5]	Unavailable	Unavailable

						Combo/d: 0.65 mg FA + 12.2 mg Pyridoxine + 0.4 mg Cobalamin (n=20)			
Ubbink, JB. 1993 [89]	Dietary intervention trial	20 men Age: 18-65[7] South Africa	1000 µg FA/d for 6 wks	Plasma folate	Radioimmunoassay (Becton Dickinson, New York, USA)	**Baseline:** 1000 µg FA/d (n=20)	5.3 ± 1.4[5]	Unavailable	Unavailable
						Intervention : 6 wks 1000 µg FA/d (n=20)	13.1 ± 5.5[5]	Unavailable	Unavailable
Ubbink, JB. 1993 [90]	Double-blind, randomized, placebo-controlled trial	30 men Age: 19-71[7] South Africa	1000 µg FA/d for 6 wks	Plasma folate	Radioimmunoassay (Becton Dickinson, New York, USA)	**Baseline:** 1000 µg FA/d (n=15)	5.6 ± 3.3[5]	Unavailable	Unavailable
						Intervention: 4 wks 1000 µg FA/d (n=15)	27.4 ± 13.8[5]	Unavailable	Unavailable
						Intervention: 6wks 1000 µg FA/d (n=15)	23.6 ± 14.6[5]	Unavailable	Unavailable
						Intervention: 8wks 2000 µg FA/d (n=15)	39.3 ± 21.9[5]	Unavailable	Unavailable
Ubbink, JB. 1995 [91]	Dietary intervention trial	30 men Age: 19-24[7] Pretoria, South Africa	1000 µg FA/d for 6 wks	Plasma folate	Radioimmunoassay (Becton Dickinson, New York, USA)	**Baseline:** Whites: 1000 µg FA/d (n=18) Blacks: 1000 µg FA/d (n=12)	8.3 ± 2.5[5] 7.7 ± 3.7[5]	Unavailable	Unavailable
						Intervention: 6 wks Whites: 1000 µg FA/d (n=18) Blacks: 1000 µg FA/d (n=12)	27.4 ± 11.8[5] 24.6 ± 15.1[5]	Unavailable	Unavailable
Undas, A. 1999 [92]	Dietary intervention trial	17 volunteers (6 women, 11 men) with elevated fasting Plasma Hcy levels Age: 22-60[7]	5 mg FA/d for 8 weeks	Plasma foalte	Radioimmunoassay (Becton Dickinson, New York, USA)	**Baseline:** 5 mg FA/d (n=17)	8.6 (3.1, 18.9)[9,11]	Unavailable	Unavailable
						Intervention: 8 wks 5 mg FA/d (n=17)	55.8 (32.0, 66.3)[9,11]	Unavailable	Unavailable
Venn, BJ. 2002 [93]	Double-blind, randomized placebo-controlled trial	104 women of childbearing Age:18-49[7] Dunedin, New Zealand	100 µg FA/d for 24 wk	RBC and Plasma folate	Microbiologic- *L. casei*	**Baseline:** 100 µg FA/d (n=31)	25.2 ± 11.5[5]	932 ± 311[5]	Unavailable
						Intervention: 24 wks 100 µg FA/d (n=31)	34.8[18]	1131.2[18]	Unavailable
Venn, BJ. 2002 [94]	Double blind, randomized placebo-controlled trial	70 males and females Age: >18 Dunedin, New Zealand June-September 1999	Daily consumption of fortified cereal for 100, 200 or 300 µg FA for 4 weeks	Serum folate	Chemiluminescence (ACS180, Ciba Corning E, Massachusetts, USA)	**Baseline:** 100 µg FA/d (n=19) 200 µg FA/d (n=22) 300 µg FA/d (n=14)	18 (14, 22)[19] 17 (14, 20)[19] 18 (15, 22)[19]	Unavailable	Unavailable
						Intervention: 4 wks 100 µg FA/d (n=19) 200 µg FA/d (n=22) 300 µg FA/d (n=13)	23 (19, 28)[19] 28 (23, 33)[19] 33 (29, 38)[19]	Unavailable	Unavailable

Venn, BJ. 2003 [95]	Randomized, placebo-controlled study	167 healthy volunteers Age: >18 Dunedin and Balclutha, New Zealand March-April 2001	100 µg FA/d for 24 weeks or placebo	RBC and Plasma folate	Microbiologic- *L. casei*	**Baseline:** 100 µg FA/d (n=52)	23.3 (20.5, 26.5)[17]	915 (838, 999)[17]	211 (182, 244)[17]
						Intervention: 8 wks 100 µg FA/d (n=52)	28.9 (25.8, 32.4)[17]	999 (924, 1079)[17]	Unavailable
						Intervention: 16 wks 100 µg FA/d (n=52)	28.5 (24.6, 33.1)[17]	1057 (959, 1164)[17]	Unavailable
						Intervention: 24 wks 100 µg FA/d (n=52)	34.5 (30.5, 39.0)[17]	1137 (1053, 1227)[17]	Unavailable
Vermeulen, EGJ. 2000 [96]	Randomized, placebo-controlled trial	158 healthy siblings of 167 patients with premature atherothrombotic disease. Netherlands April 1993-January 1995	5 mg FA/d for 2 years	Plasma folate	Radioassay (Becton Dickinson, New York, USA)	**Baseline:** 5 mg FA/d (n=78)	12.1 ± 10.1[5]	Unavailable	Unavailable
						Intervention: 1 year 5 mg FA/d (n=72)	164.6 ± 229.1[5]	Unavailable	Unavailable
						Intervention: 2 year 5 mg FA/d (n= 68)	200.7 ± 300.9[5]	Unavailable	Unavailable
Vliet, T. 2007 [97]	Randomized, double-blinded, placebo-controlled, parallel trial	150 healthy volunteers Age: 18-66[7] Netherlands	Intervention: 6 weeks 200 µg FA/d or 400 µg FA/d	Serum folate	Competitive protein binding (Simultrac radioassay, ICN Pharmaceuticals Diagnostic, New York, USA)	**Baseline, male:** 200 µg FA/d (n=27) 400 µg FA/d (n=24)	15.4 ± 6.0[5] 15.8 ± 3.5[5]	Unavailable	196 ± 53[5] 220 ± 55[5]
						Intervention 4 wks, male: 200 µg FA/d (n=27) 400 µg FA/d (n=24)	21.3[18] 26.9[18]	Unavailable	Unavailable
						Intervention 6 wks, male: 200 µg FA/d (n=27) 400 µg FA/d (n=24)	22.9[18] 30.3[18]	Unavailable	Unavailable
						Baseline, female : 200 µg FA/d (n=22) 400 µg FA/d (n=24)	16.1 ± 5.7[5] 13.7 ± 5.0[5]	Unavailable	178 ± 54[5] 186 ± 61[5]
						Intervention 4 wks, female: 200 µg FA/d (n=21) 400 µg FA/d (n=24)	22.8[18] 28.5[18]	Unavailable	Unavailable
						Intervention 6 wks, female: 200 µg FA/d (n=22) 400 µg FA/d (n=24)	25.5[18] 33.7[18]	Unavailable	Unavailable
Von Der Porten, AE. 1992 [98]	Dietary intervention trial	6 Caucasian men Age: 22-31[7]	1600 µg FA/d for 4 wks	Serum and RBC folate	Microbiologic- *L. casei*	**Baseline:** 1600 µg FA/d (n=6)	18[18]	501[18]	Unavailable
						Intervention: 4 wks 1600 µg FA/d (n=6)	45[18]	750[18]	Unavailable

Voutilainen, S. 2003 [99]	Double-blind, randomized controlled trial	20 healthy males Age: 25.2 ± 3.8[5] Kuopio, Finland	900 µg FA/d for 12 wks	Plasma folate	Radioimmunoassay (Quanta phase II, Bio-Rad, California, USA)	**Baseline:** 900 µg FA/d (n=20)	8.8 ± 3.3[5]	Unavailable	Unavailable
						Intervention: 12 wks 900 µg FA/d (n=20)	34.9 ± 25.6[23]	Unavailable	Unavailable
Wald, DS. 2001 [100]	Randomized, placebo-controlled trial	151 patients with ischemic heart diesease Chichester, England	0.2, 0.6, 0.8 or 1.0 mg/d for 3 mo	Serum folate	Microbiologic- *L. casei*	**Baseline:** Overall (n=151, includes placebo) 0.2 mg FA/d (n=27) 0.4 mg FA/d (n=25) 0.6 mg FA/d (n=25) 0.8 mg FA/d (n=25) 1.0 mg FA/d (n=24)	15.4[24], 18.4[18]	Unavailable	Unavailable
						Intervention: 3 mo 0.2 mg FA/d (n=26) 0.4 mg FA/d (n=24) 0.6 mg FA/d (n=25) 0.8 mg FA/d (n=25) 1.0 mg FA/d (n=24)	 10.2[25] 26.1[25] 31.5[25] 46.0[25] 55.3[25]	Unavailable	Unavailable
Wang, L. 2015 [101]	Double-blind, randomized controlled trial	390 healthy participants Age: 60-74[7] Hebei province, China July 2007-September 2012	400 µg FA for 12 months	Plasma folate	Microbiologic- *L. casei*	**Baseline:** 400 µg FA (n=195)	9.9 (9.2, 10.6)[17]	Unavailable	Unavailable
						Intervention: 6 mo 400 µg FA (n=180)	38.6[26]	Unavailable	Unavailable
						Intervention: 12 mo 400 µg FA (n=173)	37.2[26]	Unavailable	Unavailable
Ward, M. 1997 [102]	Crossover, dietary intervention trial	30 healthy male volunteers, Age: 34-65[7] Londenderry, Northern Ireland	100 µg FA/d for 6 wks; 200 µg FA/d for next 6 wks; 400 µg FA/d for next 14 weeks	Serum and RBC folate	Microbiologic- *L. casei*	**Baseline:** baseline (n=30)	17.5 ± 10.4[5,9]	1060.1 ± 385.9[5]	Unavailable
						Intervention: 6 wks 100 µg FA/d (n=30)	20.7 ± 7.9[5,9]	Unavailable	Unavailable
						Intervention: 12 wks 200 µg FA/d (n=30)	25.2 ± 7.9[5,9]	Unavailable	Unavailable
						Intervention: 26 wks 400 µg FA/d (n=30)	39.0 ± 10.9[5,9]	1411.9 ± 397.3[5]	Unavailable
Williams, E. 2005 [103]	Placebo-controlled, crossover trial	10 males Age: 32[18] Ulster, Northern Ireland	100 µg/d FA for 6 weeks	RBC and Serum folate	Microbiologic- *L. casei*	**Baseline:** 100 µg/d FA (n=10)	9.9 ± 7.3[5]	969.3 ± 525.9[5]	Unavailable
						Intervention: 6 weeks 100 µg/d FA (n=10)	10.6[18]	1405.5[18]	Unavailable
Winkels, R. 2008 [104]	Randomized control trial	143 healthy males and females Age: 50-75[7] Netherlands	Daily consumption of fortified bread for 138 µg FA/day for 12 wks	RBC and Serum folate	Chemiluminescence immuoassay (Access Immunoassay, Beckman Coulter)	**Baseline:** 138 µg FA/day	15.7 ± 6.0[5]	n/a[10]	Unavailable

						Intervention: 12 wks 138 µg FA/day	20.2 ± 6.6[5]	n/a[10]	Unavailable
Wolters, M. 2005 [105]	Randomized control trial	220 healthy females Age: 60-91[7] Hanover , Germany	Daily consumption of multivitamin that contains 400 µg FA for 6 mo	RBC and Serum folate	Chemiluminescence system (ACS:180, Chiron Diagnostics, Fernwald, Germany)	**Baseline:** Multivitamin group (400µg FA/d) (n=108)	20.3 (12.5, 34.3)[27]	n/a	317 ± 86.2[5]
						Intervention: 6 mos Multivitamin group (400µg FA/d) (n=92)	58.9 (35.0, 89.5)[27]	n/a	Unavailable
Woo, KS. 2002 [106]	Dietary intervention trial	29 healthy adults with hyperhomocysteineimia, Age: 52± 8[5] Hong Kong	10 mg FA/d for 1 year	Plasma folate	Immunoassay (DPC dual-count solid-phase no-boil kit, Diagnostics Products Corporation, California, USA)	**Baseline:** 10 mg FA/d (n=29)	24 ± 5[5]	Unavailable	Unavailable
						Intervention: 1 year 10 mg FA/d (n=29)	40 ± 5[5]	Unavailable	Unavailable
Wright, A. 2010 [107]	Placebo-controlled Intervention Trial	163 healthy males and females Age: 18-65 United Kingdom	**Intervention:** Natural food folate and 200µg/d FA supplement feeding study (16 wks)	RBC and Plasma folate	Microbiologic- *L. casei*	**Baseline:** FA: (n=40)	24.1 ± 2.4[6]	833 ± 56[6]	711 ± 36[6]
						Intervention: 16wks FA: (n=40)	43.06[18]	1,154[18]	666.6 ± 30.8[6]
Zheng, S. 1989 [108]	Dietary intervention trial	150 healthy subjects Linxian, China	400 µg FA/d for 16 wks	RBC folate	Microbiologic- *L. casei*	**Baseline:** 400 µg FA/d (n=100)	Unavailable	449.5 ± 193.0[5,9]	Unavailable
						Intervention: 16wks 400 µg FA/d (n=88)	Unavailable	735.5 ± 340.5[5,9]	Unavailable

[1]Excepting unit conversions, all data in tables are as published in the literature or as provided by authors in correspondence. Data included in the meta-analyses may differ as discussed in the statistical methods.
[2]FA, folic acid; mo, months; wks, weeks; MZ, monozygotic; DZ, dizygotic
[3]Population characteristics (if given) as presented in the original paper (unless noted otherwise); sample size; age (in years); sampling description; ethnicity/nationality; study location; data collection periods
[4]Blood folate assay method: assay method; organism (if relevant); assay name (if given); manufacturer (if given)
[5]Mean ± SD
[6]Mean ± SEM
[7]Range
[8]Median (interquartile range)
[9]Values reported in µg/L or ng/mL and converted to nmol/L using: 1 µg/L=2.226 nmol/L
[10]Paper presented RBC folate data, but blood folate assay method used was not microbiologic
[11]Median (range)
[12]Mean increase from baseline (95% confidence interval)
[13]Median change from baseline (IQR)
[14]Geometric mean (range)
[15]Mean ± SD (geometric mean)
[16]Mean (95% confidence interval)
[17]Geometric mean (95% confidence interval)
[18]Mean
[19]Geometric mean (geometric SD)

[20]Least square mean (95% confidence interval)
[21]Geometric mean (minimum-maximum)
[22]Mean (interquartile range)
[23]Mean increase from baseline (SD)
[24]Median
[25]Median change from baseline
[26]Geometric mean
[27]Median (5^{th}, 95^{th} percentil

Table S2. Risk of bias (ROB) assessment tool questions by study design, as adapted from the *Item Bank for Assessment of Risk of Bias and Precision for Observational Studies*

Question followed by criteria for ranking each item as low, medium or high risk of bias	**Cohort**	**Case-Control**	**Cross-sectional**
SELECTION BIAS			
Clear inclusion/exclusion criteria: 1. *Does the article clearly state its own inclusion/exclusion criteria (i.e., does not require the reader to infer)?* **Low**: Clearly states and defines (as appropriate) excluded groups **Moderate**: Criteria partially stated or stated but not adequately defined (e.g., states that only healthy subjects are included but does not define healthy) **High**: Criteria not stated	X	X	X
Appropriate sample selection: 2. *Is the sample appropriate?* **Low**: Exclusion of unhealthy individuals and population-based **Moderate**: —Exclusion of unhealthy individuals but not population-based **High**: Non-exclusion of unhealthy individuals and not population-based	X	X	X
DETECTION BIAS			
Valid assessment of inclusion/exclusion: 3. *Are the inclusion/exclusion criteria measured using valid and reliable measures?* **Low**: Physical exam, lab test, or other measure to verify "healthy, pregnancy status, or WCBA " status; survey of nationally-representative sample **Moderate**: Self-report (questionnaire or interview); stated as healthy population but undefined **High**: Inappropriate tool used in assessment of criteria	X	X	X
Valid assessment of exposure: 4. *Is the level of detail in describing the intervention or exposure adequate?* **Low**: Provided intervention/intake information assessment method (i.e., dose, frequency) and included pill count or other compliance estimates, e.g., percent of compliance **Moderate**: Provided intervention/intake information assessment method (i.e., dose, frequency); mentioned that they monitor pill use or other compliance estimates but did not include the percent of compliance in the manuscript **High**: Included dose/frequency but no information provided regarding compliance assessment method	X	X	X
Valid assessment of outcome: 5. *Are outcomes (blood folate concentrations) assessed using valid and reliable measures, implemented consistently across all study participants?* **Low**: Microbiologic assay for serum/plasma and/or RBC folate **Moderate**: Any protein-binding assay for serum/plasma folate. **High**: Protein-bind assay for RBC folate; unknown assay 6. *Are sample storage conditions appropriate?*	X	X	X

Question followed by criteria for ranking each item as low, medium or high risk of bias	Cohort	Case-Control	Cross-sectional
Low: If storage T ≤ -70ºC **High:** If storage > -70ºC or storage temperature not specified			
ATTRITION BIAS			
Incomplete outcome data: *7. Is attrition >20%?* **Low**: No **Moderate**: Attrition >20% but paper provides description of participants lost to follow-up **High**: Attrition >20% and paper provides no description of participants lost	X	N/A	N/A

Table S3. Summary risk of bias tables for randomized controlled trials using Cochrane tool[1] and for non-randomized controlled trials and observational studies using adapted RTI item bank.

First Author	**Selection bias**		**Detection bias**				**Attrition bias**	**Overall Risk of Bias[1]**
Domains / **Papers**	Clear inclusion/ exclusion criteria[2]	Appropriate sample selection	Valid assessment of				Incomplete outcome data	
			Inclusion/ exclusion	Exposure[2]	Outcome for assay[2]	Outcome for storage[2]		
Aarabi, M. 2015	L	M	M	H	L	H	L	H
Adank, C. 2003	L	M	L	M	L	L	L	M
Amatayakul, K. 1984	L	M	M	M	M	H	L	H
Anderson, C. 2010	L	M	M	L	M	L	L	M
Anderson. C. 2013	L	M	M	L	M	H	H	H
Ashfield-Watt, P. 2001	L	M	L	M	M	H	L	H
Ashfield-Watt, P. 2002	L	M	L	H	M	L	L	H
Baro, L. 2003	L	M	L	M	M	L	L	M
Baro, L. 2004	L	M	L	M	M	L	H	H
Basoglu, C. 2009	L	M	L	H	M	H	L	H
Biswas, A. 2009	L	M	L	H	M	L	L	H
Bramswig, S. 2009	L	M	L	L	L	H	L	H
Bronstrup, A. 1998	H	H	H	M	M	H	L	H
Brouwer, I. 1998	L	M	L	M	M	H	L	H
Brouwer, I. 1999	L	M	M	L	M	H	L	H
Brouwer, I. 2000	L	M	M	M	M	H	L	H

Carlsson, CM. 2004	L	M	M	L	M	H	M	H
Cheong, M. 2016	L	M	L	L	L	L	L	M
Cotlarciuc, I. 2011	L	M	M	M	M	H	L	H
Cuskelly, GJ. 1996	L	M	M	M	L	H	H	H
Daly, S. 2002	L	M	L	L	L	H	M	H
Davis, BA. 1995	L	M	L	M	L	H	L	H
Deshmukh, U. 2010	L	M	L	L	L	L	L	M
Dierkes, J. 1998	L	M	L	L	M	H	L	H
Doshi, S. 2003	L	M	L	H	M	H	L	H
Doshi, SN. 2002	L	M	L	L	M	L	L	M
Dragani, A. 2010	L	M	L	M	M	L	L	M
Durga, J. 2007	L	M	L	L	M	L	L	M
Duthie, S. 2010	L	M	L	H	M	H	L	H
Earnest, C. 2002	M	H	M	H	L	L	L	H
Ebisch, IMW. 2006	L	M	L	L	M	H	L	H
Fohr, I. 2002	L	M	L	L	M	H	L	H
Gamble, M. 2006	H	H	M	L	M	L	L	H
Green, T. 2005	L	M	M	L	L	L	L	M
Green, T. 2013	L	M	L	M	L	L	L	M
Green, TJ. 2003	L	M	L	H	L	H	L	H
Grieger, J. 2009	L	M	M	M	M	L	L	M
Haglund, O. 1993	L	M	L	M	M	L	L	M
Hao, L. 2008	L	L	L	L	L	L	L	L
Herrmann, M. 2006	M	M	M	H	M	H	L	H
Heseker, H. 1987	M	M	M	H	M	H	L	H
Heseker, H. 1993	M	M	M	H	M	L	H	H
Hiraoka, M. 2004	M	M	M	H	M	H	L	H
Holmes, T. 2003	L	M	M	M	M	H	L	H
Hursthouse, N. 2011	L	M	M	L	L	L	L	M
Johansson, M. 2002	L	M	L	H	M	H	L	H

Kauwell, G. 2000	L	M	L	L	L	H	L	H
Klerk, M. 2004	L	M	L	L	M	L	L	M
Kok, DEG. 2015	L	L	L	H	M	H	L	H
Lamers, Y. 2004	L	L	L	L	M	H	L	H
Liem, A. 2003	L	M	L	H	M	H	L	H
Lin, P. 2006	L	M	L	L	M	H	L	H
Mann, BA. 1987	H	H	H	M	M	L	H	H
Mao, G. 2008	L	M	L	M	M	L	L	M
Martin-Bautista, E. 2010	L	M	L	L	M	L	L	M
McKay, DL. 2000	L	L	L	L	M	L	M	M
Meer, K. 2005	L	M	L	L	M	L	L	M
Melse-Boonstra, A. 2004	L	M	L	L	M	L	L	M
Nguyen, P. 2008	L	L	L	L	L	L	L	L
Nguyen, P. 2009	L	M	L	L	L	L	L	M
Norsworthy, B. 2001	L	M	L	M	L	H	L	H
Olthof, M. 2006	L	M	L	L	M	L	L	M
Oort, F. 2003	L	M	L	L	M	L	L	M
Papandreou, D. 2010	H	H	L	H	M	H	L	H
Pathansali, R. 2006	L	M	L	H	M	H	L	H
Pena, A. 2007	L	M	L	L	M	H	L	H
Petrogianni, M. 2012	L	M	L	M	M	L	L	M
Pinto, X. 2005	L	M	L	M	M	H	L	H
Pullin, CH. 2001	L	M	L	M	M	L	L	M
Qin, X. 2012	L	M	L	L	M	L	L	M
Quinlivan, EP. 2002	L	M	L	H	L	H	L	H
Raigani, M. 2014	L	M	L	H	M	H	L	H
Rhode, BM. 1983	L	M	M	M	L	H	L	H
Rosenthal, J. 2008	L	M	L	M	M	H	M	H
Schorah, CJ. 1998	L	M	M	H	M	H	L	H
Sharifi, F. 2010	L	L	L	H	M	H	L	H

Sheu, W. 2005	L	M	L	L	M	L	L	M
Shidfar, F. 2009	L	M	L	H	M	H	L	H
Smidt, LJ. 1990	L	L	L	L	L	H	L	H
Strandhagen, E. 2003	L	M	L	H	M	L	L	H
Sweeney, MR 2007	L	M	M	M	L	H	L	H
Tapola, NS. 2004	L	L	L	L	M	H	L	H
Tighe, T. 2011	L	M	L	L	L	H	L	H
Title, L. 2000	L	M	L	L	M	L	L	M
Toprak, A. 2005	L	M	L	L	M	H	L	H
Tsui, JC. 1990	L	M	L	L	M	H	M	H
Tucker, K. 2004	L	M	M	L	M	L	L	M
Ubbink, J. 1994	L	M	L	M	M	L	L	M
Ubbink, JB. 1993	L	M	L	H	M	H	L	H
Ubbink, JB. 1993	L	M	L	H	M	H	L	H
Ubbink, JB. 1995	L	M	L	L	M	H	L	H
Undas, A. 1999	L	M	L	H	M	L	L	H
Venn, BJ. 2002	L	M	M	M	L	H	L	H
Venn, BJ. 2002	L	M	L	M	L	H	L	H
Venn, BJ. 2003	L	L	M	L	L	L	L	M
Vermeulen, EGJ. 2000	L	L	L	L	M	L	L	M
Vliet, T. 2007	L	M	L	L	M	H	L	H
Von Der Porten, AE. 1992	L	M	L	M	L	H	L	H
Voutilainen, S. 2003	L	M	L	M	M	L	L	M
Wald, DS. 2001	L	M	M	L	L	H	L	H
Wang, L. 2015	L	M	M	L	L	L	L	M
Ward, M. 1997	L	M	M	M	L	H	L	H
Williams, E. 2005	L	M	L	M	L	L	L	M
Winkels, R. 2008	L	M	L	L	M	L	L	M
Wolters, M. 2005	L	M	M	M	M	H	L	H
Woo, KS. 2002	L	M	M	L	M	L	L	M

Wright, A. 2010	L	M	L	H	L	H	L	H
Zheng, S. 1989	H	M	H	L	L	H	L	H

[1] Risk of bias assessment: L = low; M = moderate; H = high

[2] Cochrane recommends stating potential sources of bias not addressed in the other domains of the risk of bias tool. Additional potential sources of bias identified in our systematic review include clear inclusion/exclusion criteria across comparison groups, and valid assessments for exposure and outcome (assay used and sample storage conditions)

Protocol: Folic acid supplementation and blood folate concentration – a systematic review and meta-analysis

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Research question
How does folic acid intake change blood folate concentrations?

Objective
To perform a systematic review and meta-analysis of impact of folic acid supplementation on and blood folate concentrations

Methods
Search strategy
A research librarian from the CDC Public Health Library will be consulted and will perform the literature search using the following search terms (adapted for databases as necessary) for English language literature published between January 1980 - October 2014.

We will use the following search strategy to search Embase and adapt as required for other electronic databases:

1. Folic acid.mp or folic acid/
2. Blood folate.mp or exp folic acid blood level/
3. (Serum folate or plasma folate or red blood cell folate or erythrocyte folate).mp
4. (Intake or diet* or supplement*).mp
5. Folic acid intake.mp
6. Limit 21 to (English language and yr="1980–October 2014")

In addition to Embase, the following databases will be searched: Cochrane Library, CINAHL, POPLINE, PubMed, and Web of Science

To identify additional resources, we will search the references of all articles in the full text review.

If supplement use stratified data or other population information is needed for eligibility in the review, we will contact authors for additional information.

Inclusion criteria

- All studies will be considered, with the exception of case studies and cross sectional studies:
    - Randomized trials, quasi-randomized, and non-randomized control trials with individual or cluster level randomization.
    - Supplementation trials without placebo control will be included (although evaluated in sensitive analysis.)

Exclusion criteria

- Studies that do not contain information on the relationship between at least two of the four following outcome measures: e.g., must be able to calculate change in blood folate concentrations (concentration after XX days/weeks/months/years - baseline concentration – before known dose of folic acid was administered).
    - Serum/plasma folate or red blood cell (RBC), erythrocyte folate at baseline and during intervention
    - Folic acid intake dose

- Studies including unhealthy populations, defined as sample recruitment based on a health condition.
    - Including, but not limited to: conditions impacting folate absorption, such as intestinal malabsorption conditions, inflammatory bowel disease, alcohol abuse, cancer, chronic congestive heart failure, chronic renal failure, chronic liver failure, or chronic infectious disease.
- Studies in pregnant, lactating.
- Studies without blood folate concentrations stratified by folic acid containing supplement use.

Selection of studies

Excel will be used to store all identified studies from the search strategy. Titles and abstracts will be screened in duplicate. Three teams of two review abstracts and full text files (KSC+YPQ, YPQ+IZ, and KSC+AS).

Data extraction

For eligible studies, two reviewers will independently extract 1/3 of data using a piloted abstraction form. Any discrepancies will be resolved through discussion and document the process.

The following information will be extracted from each study:

1. Methods
    - Study design
    - Folate assay method
2. Participants
    - Location of the study
    - Data collection time frame
    - Sample size
    - Age
    - Blood folate concentrations
    - Natural food folate intake
    - Method of dietary assessment
3. Intervention
    - Folic acid dose
    - Folate intake if provided/reported
    - Duration of the intervention specify for each data point

Risk of bias

Two review authors (YPQ, KSC) developed and adapted tools for the assessment of risk of bias. For control trials, the *Cochrane Handbook for Systematic Reviews of Interventions* was used [109]. For observational studies, an adapted Item Bank on Risk of Bias and Precision of Observational Studies from the Research Triangle Institute (RTI) was used [110]. LFY and KSC will independently evaluate risk of bias for each study for the domains below.

Domain risk of bias

A score of low, moderate, and high risk of bias score will be assigned to each domain for each study outcome (i.e. serum/plasma folate and RBC folate concentrations). Domains will be considered low risk of bias if all questions within a domain are graded as low, moderate risk of bias if one or more questions are graded as moderate or high risk of bias if one or more questions are graded as high. If we are unable to determine a domain's risk of bias due to insufficient information provided in a study, the domain will be classified as "unclear" in the risk of bias tables.

Overall risk of bias

This same convention will be applied across domains to assign an overall summary score of low, moderate, or high risk of bias for each study outcome (i.e., serum/plasma folate and RBC folate concentrations).

Control trial domains:

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome bias
- Reporting bias
- Other sources of bias (as needed)

Observational study domains:

- Uniform and valid measures of inclusion/exclusion criteria
- Appropriateness of study sample
- Exposure and outcome assessment methods
- Appropriate follow-up time[1]
- Completeness of outcome data[1]
- Adjustment for potential confounding

Data analysis

Meta-analyses

- A statistician (OJD) will use Open BUGS 3.2.2 software as statistical software.
- A Bayesian Markov Monte Carlo chain procedure will be used to develop posterior distributions

[1] Appropriate follow-up time and completeness of outcome data will not be assessed for cross-sectional studies.

    - Estimates of change over doses of folic acid between 100 µg/day to 4000 µg/day are anticipated. Changes at 4, 12, and 24 weeks of supplementation will be models.
    - Dose-response curves will then be extrapolated to a homoeostatic state (steady state) for each individual dose and those used to create a steady state response.
    - The steady state response will be compared to estimates from cross-sectional studies of fortified countries in post hoc analysis (e.g. NHANES US)
- A Bayesian Markov Monte Carlo chain procedure will be used to develop posterior distributions.
    - Each study will be treated as a random effect.
    - The percent change in blood folate concentrations for every doubling of natural food folate intake will be calculated.
- Sensitivity analyses performed will depend on the number of studies eligible for inclusion in the meta-analyses. Anticipated sensitivity analyses of the association of natural food folate intake and blood folate concentrations may be stratified by:
    - Study quality (risk of bias, study tiers)
    - Assay type
    - Study design
    - Country fortification policy status
    - Baseline folate status

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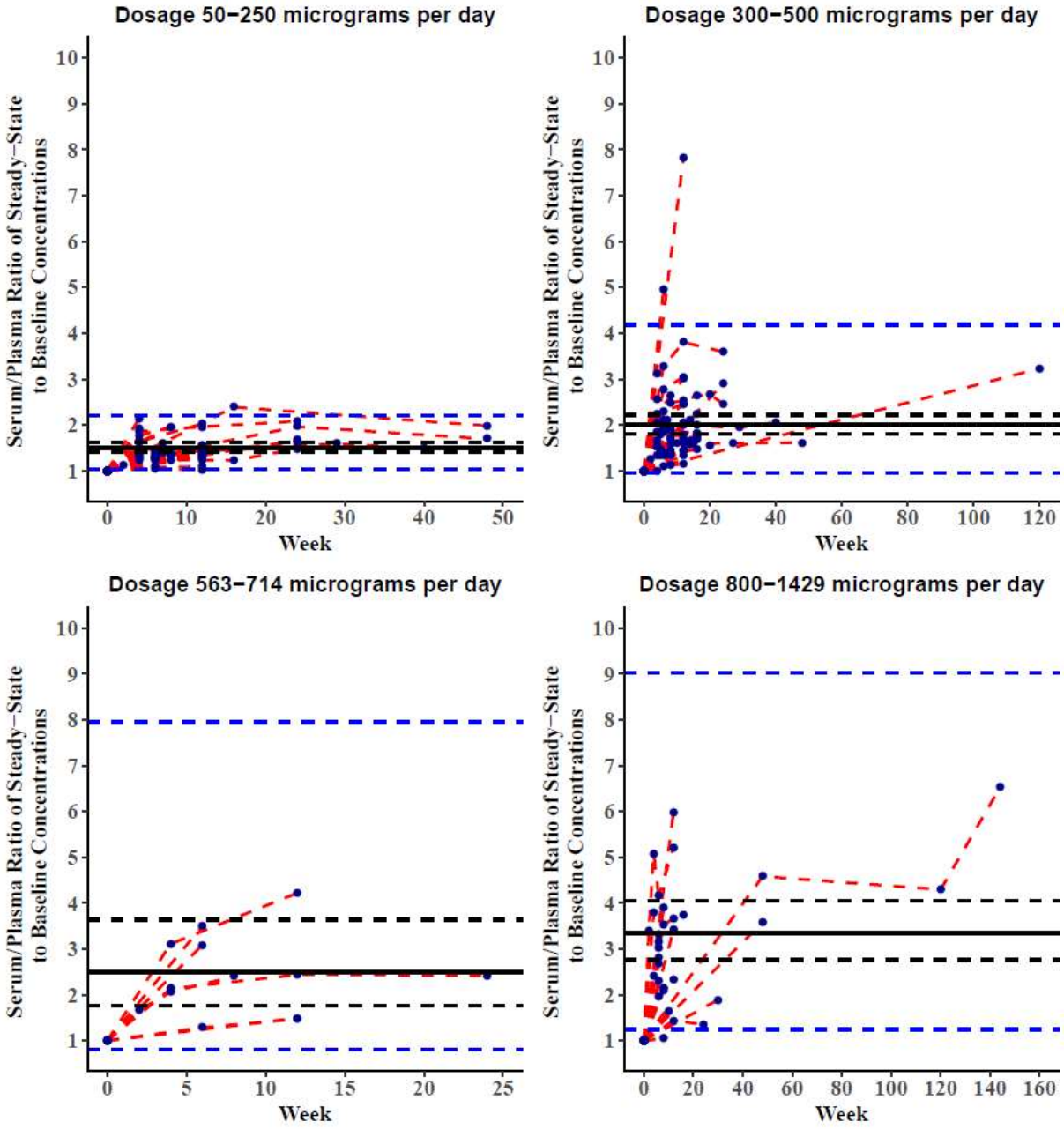

Figure S1: Fold change in serum/plasma folate concentrations from baseline over time in weeks for each study extracted. Blue dots: each data point. Black line: the estimated fold change at steady-state. Black dashed lines: 95% crediable intervals. Blue dashed lines: 95% posterior predictive intervals.

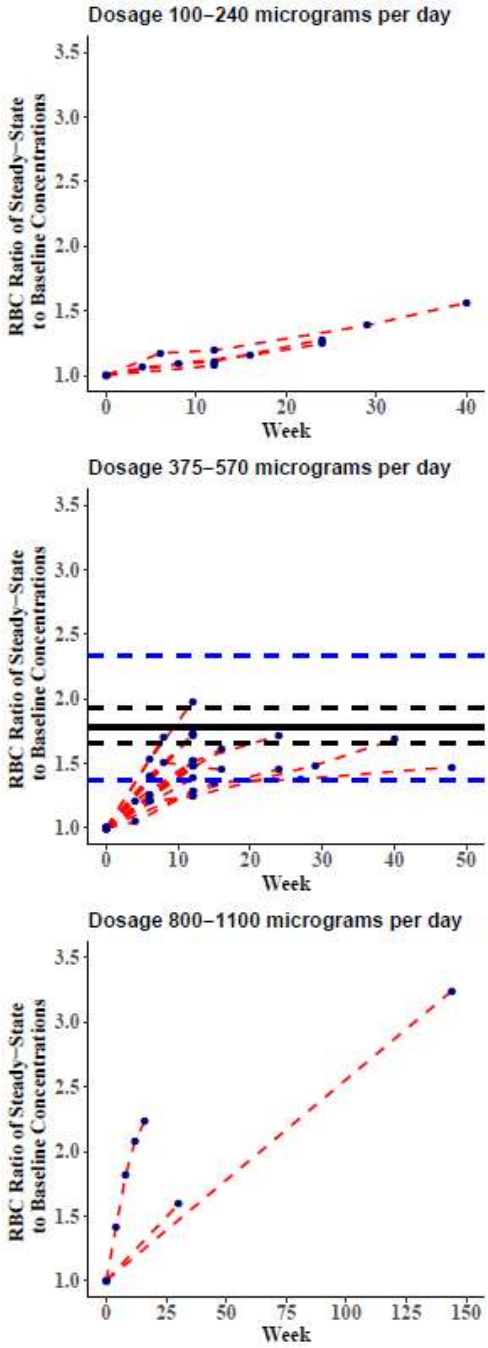

Figure S2: Fold change in red blood cell (RBC) folate concentrations from baseline over time in weeks for each study extracted. Blue dots: each data point. Black line: the estimated fold change at steady-state. Black dashed lines: 95% crediable intervals. Blue dashed lines: 95% posterior predictive intervals.