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| Table 1. Summary of the studies included in this meta-analysis |
|  | **Author** | **Year of publication** | **Sample size (N)** | **Age of subjects (years)** | **Study population** | **Exclusion criteria** | **Intervention** | **Time to follow-up** |
| **Studies on B12** | Dangour (28) | 2011 | Placebo n=75Treatment n=80 | ≥75, mean 80.0 | Community-dwelling individuals from 10 general practices in the South East of England with B12 concentrations between 107-210 pmol/l and Hb ≥ 11 g/dl (women) or ≥ 12 g/dl (men) | Diabetes, dementia, pernicious anaemia requiring B12 treatment, alcohol addiction, history of epilepsy, implanted metallic devices, current use of vitamin B12 supplements or vitamin B12 use in last 6 months | Daily tablet with 1 mg vitamin B12 during 12 months | 12 months |
| Favrat (29) | 2011 | Placebo n=22Treatment n=23 | Mean 69, median 75 | Patients from 13 private practices in the western part of Switzerland with serum vitamin B12 concentrations between 125-200 pmol/L. Participants were enrolled between October 2002 and September 2004. | Folate deficiency, renal insufficiency, folic acid or vitamin B12 treatment during preceding 6 months | Daily tablet with 1000 µg vitamin B12 during 4 weeks | 4 weeks and 4 months |
| Hvas (30) | 2001 | Placebo n=70Treatment n=67 | Mean 70 | Subjects in Aarhus, Denmark, with elevated methylmnalonic acid (P-MMA, 0.40-2.00 µmol/L) which had not received prior vitamin B12 treatment. Participants were enrolled between November 1998 and March 2000. | Low Hb concentrations, low ferritin concentrations, TSH≥4.1 mIU/L, high creatinine concentrations, life-threatening disease, treatment with anticoagulants, tropical ataxic neuropathy | Weekly 1 mg vitamin B12 intramuscular during 4 weeks | 3 months |
| Seal (31) | 2002 | Placebo n=14Treatment 1 n=12 Treatment 2 n=14 |  | Patients in two geriatric hospitals in Melbourne, Australia with subnormal serum vitamin B12 (100-150 pmol/L) discovered as part of their clinical assessment | Known neoplasm, life-threatening or terminal illness, history of malabsorption, pernicious anaemia, anaemia of other cause, prior vitamin B12 treatment or vitamin supplementation, neurological disorder other than stroke | Daily 10 µg (treatment 1) or 50 µg vitamin B12 (treatment 2) during 4 weeks | 4 weeks |
| **Studies on folic acid** | Durga(32) | 2011 | Placebo n=407Treatment n=395 | 50-70, mean 60.3 | Men and postmenopausal women from the Netherlands recruited from municipal and blood bank registries with homocysteine concentrations between 13-25 μmol/L and serum vitamin B12 concentrations >200 pmol/L. Participants were enrolled between June 2000 and December 2001.  | Plasma total homocysteine <13 µmol/L or >25 µmol/L; serum vitamin B12 <200 pmol/L; renal, kidney or thyroid disease; use of vitamin B supplements of medications that influence folate metabolism or atherosclerotic progression; <80% self-reported compliance during 6-wk run-in period | Daily capsule with 800 µg folic acid during 3 years | 3 years |
| Pathansali (33) | 2005 | Placebo n=12 Treatment n=12 | ≥65, mean 73 | Subjects from volunteers’ database with no deficiency in folic acid or vitamin B12 | History of vascular disease, hypertension, diabetes, smoking; Mini Mental State Examination score <27/30; impaired renal function; use of vitamin supplements or drugs known to affect homocysteine of folate concentrations | Daily folic acid 5 mg during 4 weeks | 4 weeks |
| Ntaios (34) | 2009 | Placebo n=50 Intervention n=53 | Mean 73 | Patients from Internal Medicine Department with at least one cardiovascular risk factor, such as diabetes mellitus, arterial hypertension, coronary artery disease, dyslipidaemia, smoking or previous ischemic stroke. Participants were enrolled between October 2005 and February 2008. | Use of drugs which interfere with homocysteine concentrations; impaired renal function (GFR<60 ml/min); renal transplantation; malignancy; pregnancy; vitamin supplementation; prior carotid endarterectomy | Daily dose of 5 mg folic acid during 18 months | 18 months |