Objective: To test the hypothesis that the incidence of fatal coronary heart disease and cardiovascular disease in a general population is related to serum and red cell folate and vitamin B-12 concentrations.

Design: Cohort study with follow up of 29 years.

Setting: Busselton, Western Australia.

Participants: 1419 men and 1531 women aged 20 to 90 years, who were alive more than three years after their participation in the 1969 Busselton health survey. 2314 (78.4%) had no cardiovascular disease at the initial survey.

Main outcome measures: Hazard ratios for fatal coronary heart disease and cardiovascular disease in men and women according to baseline concentrations of serum and red cell folate and serum vitamin B-12.

Results: 213 men and 159 women died from coronary heart disease, and 342 men and 302 women died from cardiovascular disease. Serum and red cell folate concentrations showed a moderate positive correlation \( (r=0.26, \ P<0.001) \) but otherwise serum and red cell folate and serum B-12 concentrations were not strongly correlated with each other or with other standard risk factors. After age and standard risk factors were adjusted for, there was no independent association between folate and B-12 concentrations and death from coronary heart disease or cardiovascular disease in the full cohort or the subcohort with no cardiovascular disease at baseline. The multivariate adjusted hazard ratio for death from cardiovascular disease in the lowest versus the highest category of red cell folate concentration was 1.05 (95% confidence interval 0.77 to 1.43) in men and 1.10 (0.81 to 1.51) in women.

Conclusions: These findings do not support the hypothesis that lower folate and B-12 concentrations increase the risk of fatal cardiovascular disease in a general population. The routine use of these vitamins for preventing cardiovascular disease should await evidence from clinical trials.

What is already known on this topic

Moderate hyperhomocysteinaemia is thought to be an independent risk factor for cardiovascular disease

High homocysteine concentrations in the general population are mainly due to insufficient
Evidence linking serum or dietary folate and B vitamin levels to incident cardiovascular disease is inconclusive

**What this study adds**
A large community cohort followed for 29 years showed no independent association of baseline serum and red cell folate and serum B-12 concentrations with mortality from cardiovascular disease

Vitamin therapy to lower homocysteine concentrations should not be routinely recommended in the general population until the benefit is proved by controlled clinical trials