folic acid food fortification.[2] Similar values were found among Ontario women of reproductive age.[3]

We previously showed that plasma total homocysteine levels can be relatively insensitive for detecting vitamin B_{12} deficiency.[4] A homocysteine concentration at or above 15 μmol/L has positive and negative predictive values of 7.4% and 97.2%, respectively, for the detection of a serum vitamin B_{12} concentration below 120 pmol/L. For vitamin B_{12} levels between 120 and 150 pmol/L, the corresponding predictive values are just 6.3% and 94.0%.[4] In Fig. 1 of the article by Robertson and colleagues the mean homocysteine concentration was just 12 μmol/L even in the quartile of patients with the lowest serum vitamin B_{12} concentrations (below 203 pmol/L). Thus, it is unlikely that vitamin B_{12} deficiency could be efficiently detected on the basis of a homocysteine measurement equal to or greater than 15 μmol/L.

Their lack of use of a comprehensive and suitable definition of vitamin B_{12} leads us to question the authors' conclusions that "vitamin B_{12} deficiency is surprisingly common among patients with vascular disease" and that "low serum vitamin B_{12} levels are a major determinant of elevated homocysteine levels and increased carotid plaque area."[1] With nearly 50% of patients omitted from their major analysis, could not age and serum creatinine alone have explained some of their findings?

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In examining the relationship of serum vitamin B_{12} levels to homocysteine levels,[1] Julie Robertson and colleagues highlight the utility of homocysteine in the clinical investigation of vitamin B_{12} deficiency.

Both methylmalonic acid and homocysteine are elevated in vitamin B_{12} deficiency. The measurement of methylmalonic acid requires not readily available methods involving mass spectrometry, whereas homocysteine is readily measured in the clinical laboratory by fluorescent polarization, enzymatic assays and high-pressure liquid chromatography. There is a strong correlation between methylmalonic acid and homocysteine levels, and the sensitivity of homocysteine levels for identifying vitamin B_{12} deficiency is greater than 95%.[2–4] Measurement of creatinine, folate and vitamin B_{12} levels and the patient's response to treatment will clarify the cause of the elevated homocysteine levels. At my institution we no longer routinely offer methylmalonic acid measurement as the diagnostic efficiencies of methylmalonic acid and homocysteine seem similar for the identification of a functional vitamin B_{12} deficiency.

Robertson and associates state that 17.3% of their population (73/421 cases) had a vitamin B_{12} deficiency. Of the 50 patients in whom methylmalonic acid was measured, 59% had elevated methylmalonic acid levels, confirming a functional vitamin B_{12} deficiency. It would have been interesting to know what the homocysteine levels were in these 73 subjects and to conduct a receiver–operator curve analysis to determine the efficiency of methylmalonic acid and homocysteine for identifying vitamin B_{12} deficiency. If all the patients with elevated methylmalonic acid levels also had elevated homocysteine levels, this would support the idea that homocysteine alone (without methylmalonic acid) can be used to assess vitamin B_{12} deficiency and its response to treatment.

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Correction

A news article[1] concerning the federal government's decision not to renew funding to the Canadian Network for Vaccines and Immunotherapeutics stated that the network's early success included the "beginning of the first Canadian clinical trial for a therapeutic HIV vaccine." Although the final results of this research were presented at a conference organized by the network, the research itself was sponsored by the Canadian HIV Trials Network.

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