Supplementary Material (online publication only)

Brady et al, "Homocysteine Lowering and Cognition in CKD: The VA Homocysteine Study"

Supplementary Item S1: Formula and method for calculating reliable change (RCI) index.

The formula for calculating each participant's RCI was

$$RCI = [(X_2 - X_1) - (M_2 - M_1)]/SED$$

where

X_1 = individual initial TICSm (Telephone Interview for Cognitive Status–modified) score,

X_2 = individual 1-year TICSm score,

M_1 = placebo group mean for initial TICSm score,

M_2 = placebo group mean for 1-year TICSm score, and

SED = standard error of the difference between the TICSm group means.

The formula for calculating SED was

$$SED = [(SEM_1)^2 + (SEM_2)^2]^{1/2}$$

where

SEM_1 = placebo group standard error of measurement for initial TICSm mean, and

SEM_2 = placebo group standard error of measurement for 1-year TICSm mean.

The SEMs for the initial and 1-year TICSm means were calculated as

$$SEM = SD[(1-r)^{1/2}]$$

where

SD = standard deviation for each TICSm administration, respectively for the initial (subscript 1) and 1-year (subscript 2) administrations of the test, and

r = test-retest reliability (15 month [cf Plassman et al], r = 0.83).

The difference between X_2 and X_1 represents the change in the TICSm of an individual participant, whereas the difference between M_2 and M_1 represents the change in the placebo group. If $(M_2 - M_1) > 0$, this suggests an overall practice effect, and the individual change is corrected for the practice effect in the numerator of the RCI formula.

In a manner similar to selecting rejection regions, or *P* values, for statistical tests (cf Chelune et al), we selected upper (ie, true improvement) and lower (ie, true decline) cut-off regions equivalent to a 2-tailed test at $P < 0.1$. Accordingly, an RCI of −1.65 or lower represented reliable decline, an RCI of 1.65 or higher

represented reliable improvement, and RCIs between these values represented no change over 1 year. When calculating the RCI, we rounded the results to integers because TICSm change at the individual level is expressed only in integers. We could not examine change using the RCI procedure for the cognitive and memory outcomes because these composites were composed of z-scores from multiple tests or single items from specific tests, and RCIs are calculated using retest the reliability coefficient of individual tests.

Data from the 243 persons in the placebo group who completed initial and 1-year retests were used for the RCI calculations. The placebo group TICSm values at initial and 1-year retest were, respectively; $M_1 = 32.5$, $SD_1 = 4.7$, $M_2 = 33.0$, $SD_2 = 5.6$. The slight improvement in average scores (1.5%) after 1 year in the placebo group may have indicated a practice effect, which is a common phenomenon in cognitive function studies using repeated measures (eg, cf Kang et al).

We estimated reliable improvement and decline on the TICSm using the RCI cutoffs of ±1.65 for a 2-tailed rejection region at $P < 0.1$, similar to selecting rejection regions for statistical tests (cf Chelune et al). These cutoffs corresponded to a 1-year TICSm improvement of 6 or more points indicating improvement, a 1-year decline of 5 or more points indicating decline, and 1-year differences less than those values, respectively, indicating no change. TICSm scores had to exhibit a relatively larger 1-year increase to exceed the cutoff for reliable improvement because of the practice effect noted above.

Works Cited:

Plassman BL, Newman TT, Welsh KA, et al: Properties of the telephone interview for cognitive status: Application in epidemiological and longitudinal studies. Neuropsychiatry Neuropsychol Behav Neurol 7:235-241, 1994

Chelune GJ, Naugle RI, Lueders H, et al: Individual change after epilepsy surgery: Practice effects and base-rate information. Neuropsychol 7:41-52, 1993

Kang JH, Cook N, Manson J, Buring JE, Albert CM, Grodstein F: A trial of B vitamins and cognitive function among women at high risk of cardiovascular disease. Am J Clin Nutr 88:1602-1610, 2008