Published in final edited form as:

Ann Neurol. 2013 August ; 74(2): 307. doi:10.1002/ana.23952.

Comment on “Intakes of Vitamin C and Carotenoids and Risk of Amyotrophic Lateral Sclerosis: Pooled Results from 5 Cohort Studies”

D. Michal Freedman, Ph.D., M.P.H.¹, Ralph W. Kuncel, M.D., Ph.D.², Stephanie J. Weinstein, Ph.D.¹, and Demetrius Albanes, M.D.¹

¹ Department of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, DHHS, Bethesda, Maryland ² University of Redlands, Redlands, California

We read with interest the study by Fitzgerald et al.¹, which found an inverse association between ALS and dietary intake of beta-carotene and lutein in a pooled cohort analysis. The authors also examined vitamin C intake and vitamin C supplement use, but did not discuss the use of carotenoid supplements (neither beta-carotene nor other carotenoids). Nonetheless, some readers may conclude that supplementation with beta-carotene or other carotenoids, which would generally provide higher doses than dietary intake, might offer even greater protection against ALS. We caution against this inference, particularly because of the results of our study on the relationship between ALS and supplemental beta-carotene (and vitamin E) in a randomized clinical trial of Finnish male smokers.² This trial was initiated in the 1980s to determine whether supplementation with vitamin E or beta-carotene reduces lung cancer or other cancer incidence. Although it was not an *a priori* hypothesis of the trial, our study examined the trial results for the effects of these supplements on ALS risk. In our study, beta-carotene supplements were associated with a slightly *elevated*, although not statistically significant, risk of ALS. While the finding is not strong evidence of risk, it remains worrisome. Beta-carotene supplements have been associated with an increase in cancer at several sites.³ We therefore want to emphasize the conclusions of Fitzgerald et al. that the inverse association between ALS and beta-carotene and other carotenoids they reported was based only on dietary intake, and not on use of supplements.

References

1. Fitzgerald KC, O'Reilly EJ, Fondell E, et al. Intakes of vitamin C and carotenoids and risk of amyotrophic lateral sclerosis: Pooled results from 5 cohort studies. *Ann Neurol.* Feb. 2013; 73(2): 236–45. [PubMed: 23362045]
2. Freedman DM, Kuncel RW, Weinstein SJ, et al. Vitamin E serum levels and controlled supplementation and risk of amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration.* 2013:1–6. Early Online.

Potential Conflicts of Interest
Nothing to report

3. Albanes D, Heinonen OP, Huttunen JK, et al. Effects of alpha-tocopherol and beta-carotene supplements on cancer incidence in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study. *Am J Clin Nutr.* Dec; 1995 62(6 Suppl):1427S–30S. [PubMed: 7495243]