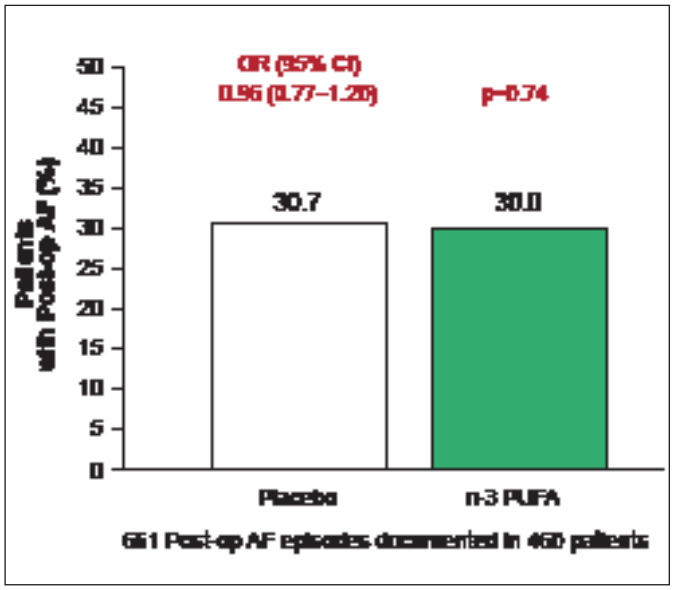
Figure 1. OPERA Primary Endpoint: Postoperative AF Episodes.



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Based on the data, Prof. Marchioli concluded that postoperative AF remains an enigmatic and difficult-to-prevent complication of cardiac surgery. While n-3 PUFA appeared to be safe and well-tolerated with no evidence of increased bleeding, the OPERA trial "provides evidence that perioperative n-3 PUFA does not appreciably reduce postoperative AF in the acute setting of cardiac surgery."

Multivitamins for the Prevention of Cardiovascular Disease in Men

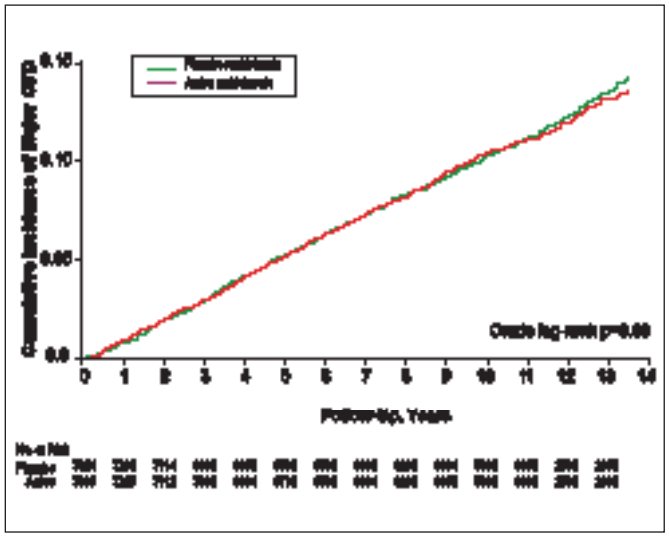
Written by ***Toni Rizzo***

Basic research has suggested that some individual vitamin and mineral components of multivitamins might reduce the risk of cardiovascular disease (CVD). However, no large-scale, long-term randomized trials have tested the effect of multivitamins. Howard D. Sesso, ScD, MPH, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented results from the Physicians' Health Study II (PHS II) on the long-term risks and benefits of multivitamin use in male physicians [Sesso HD et al. *JAMA* 2012].

PHS II was a randomized, double-blind, placebo-controlled, 2x2x2x2 factorial trial testing multivitamin, vitamin E, vitamin C, and beta-carotene. It was conducted by mail in 14,641 male physicians aged ≥50 years. A total of 7641 PHS I participants and 7000 new physicians were randomized to take an active multivitamin or its placebo, as well as for the other vitamin arms. For the multivitamin component, the primary cardiovascular (CV) endpoint was major CV events (nonfatal myocardial infarction [MI], nonfatal stroke, and CV death). The secondary endpoints were total and fatal MI, total and fatal stroke, ischemic and hemorrhagic stroke, CVD mortality, and total mortality. The participants were followed for a mean of 11.2 years, resulting in 164,000 person-years of follow-up.

Multivitamin compliance was 77% at 4 years, 72% at 8 years, and 67% at study end. Baseline characteristics were well balanced between the multivitamin and placebo groups. The cumulative incidence of major CV events at study end was not significantly different between the 2 groups (HR, 1.01; 95% CI, 0.91 to 1.10; crude log-rank p=0.69; Figure 1). Similarly, no significant differences were seen in the incidences of secondary endpoints (Table 1). There was a borderline significant reduction in MI death (27% vs 43%; HR, 0.61; 95% CI, 0.38 to 0.995; p= 0.048) that may have due to chance, given its small case counts.

Figure 1. Major CV Events: Active Versus Placebo Multivitamins During 11.2 Years of Follow-Up.



Notably, the total number of cancers—the other primary endpoint of the multivitamin component of the trial—was modestly but significantly reduced, with 1290 in the multivitamin group versus 1379 in the placebo group (HR, 0.92; 95% CI, 0.86 to 0.998; p=0.04). The total number of incident cancers among participants with a baseline history of cancer was also significantly lower in the multivitamin group (95) versus the placebo group (126; HR, 0.73; 95% CI, 0.56 to 0.96; p=0.02) but was not significantly lower among participants without a baseline history of cancer (1195 vs 1253; HR, 0.94; 95% CI, 0.87 to 1.02; p=0.15).

Table 1. Association Between Randomized Multivitamin Assignment and Risk of Major CV Events and Mortality.[a]

	Number of Events			
Outcome	Multivitamin n=7317	Placebo n=7324	Adjusted HR (95% CI)[b]	p Value
Major CV events[c]	876	856	1.01 (0.91–1.10)	0.91
Total MI[d]	317	335	0.93 (0.80–1.09)	0.39
MI death	27	43	0.61 (0.38–0.995)	0.048
Total stroke[d]	332	311	1.06 (0.91–1.23)	0.48
Stroke death	89	76	1.16 (0.85–1.58)	0.34
Ischemic stroke[e]	277	250	1.10 (0.92–1.30)	0.29
Hemorrhagic stroke[e]	49	45	1.08 (0.72–1.63)	0.69
CV death	408	421	0.95 (0.83–1.09)	0.47
Total mortality[f]	1345	1412	0.94 (0.88–1.02)	0.13

CV=cardiovascular; MI=myocardial infarction; [a]Mean follow-up of 11.2 years for all 14,641 men through June 1, 2011; [b]Adjusted for age, Physicians' Health Study (PHS) cohort (original PHS I participant, new PHS II participant), randomized beta-carotene assignment, randomized vitamin E assignment, and randomoized vitamin C assignment and stratified on CV disease at baseline; [c]Defined as a composite endpoint consisting of the first of any of the following individual events: normal MI, nonfatal stroke, and CV death. The individual events do not sum to the total because each individual analysis assess the first event that occurs during follow-up. Therefore, a participant who for example has an MI and then dies of CV disease would be counted for both individual events but only once for the primary end point of major CV events; [d]Includes both fatal and nonfatal events; [e]Stroke type was unknown for 6 men in the active multivitamin group and for 16 men in the placebo group; [f]Additionally stratified on baseline cancer.

The results of the PHS II trial demonstrated no effect of long-term multivitamin use on CVD in men. The main reason to take a daily multivitamin is still for the prevention of vitamin and mineral deficiency, along with the potential reductions on total cancer. The investigators will provide additional results on the effects of multivitamins on the secondary endpoints of eye disease and cognitive function, and other important analyses of CV and cancer outcomes, along with extended follow-up of this trial cohort.

Omega-3 Fatty Acids for the Prevention of Recurrent Symptomatic AF: Results of the FORWARD Trial

Written by ***Phil Vinall***

According to the results from the Randomized Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation [FORWARD; NCT00597220] presented by Alejandro Macchia, MD, Fundación GESICA, Buenos Aires, Argentina, pharmacological supplementation with n-3 polyunsaturated fatty acids (PUFA) does not reduce recurrent atrial fibrillation (AF).

Results from previous epidemiological studies and small clinical trials have been inconclusive regarding the ability of PUFA to reduce or prevent AF. The objective of this study was to test the efficacy of pharmacologic supplementation (1 g/day for 1 year) of n-3 PUFA for the maintenance of normal sinus rhythm in patients with previous AF.

The patient population consisted of men and women at least 21 years of age who had recovered normal sinus rhythm after having been diagnosed in an outpatient setting with symptomatic AF. Patients had either paroxysmal AF (defined as at least 2 symptomatic episodes of documented AF in the previous 6 months before randomization with the last episode occurring within 3 to 90 days before enrolling) or persistent AF (defined as successful electrical or pharmacological cardioversion performed within 3 to 90 days before study enrollment). Patients with lone AF, class IV congestive heart failure (CHF), acute coronary syndrome (ACS), or cardiac surgery in the previous 3 months were not eligible for the study. The presence of significant valvular disease, Wolff-Parkinson-White syndrome, planned or recent implantation of a cardiac device, ablative treatment for AF, or any arrhythmia associated with an acute reversible condition were also cause for exclusion.

The primary efficacy endpoint was the time to first recurrence of symptomatic or asymptomatic AF as documented by a 12-lead ECG. Secondary endpoints included the hierarchical composite of all-cause mortality, nonfatal stroke, nonfatal acute myocardial infarction, systemic embolism, CHF development, and severe bleeding; all-cause hospitalization; survival free of thromboembolic events; and hospitalization for cardiovascular reasons. Follow-up clinical visits occurred at 2, 4, 8, and 12 months.