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.

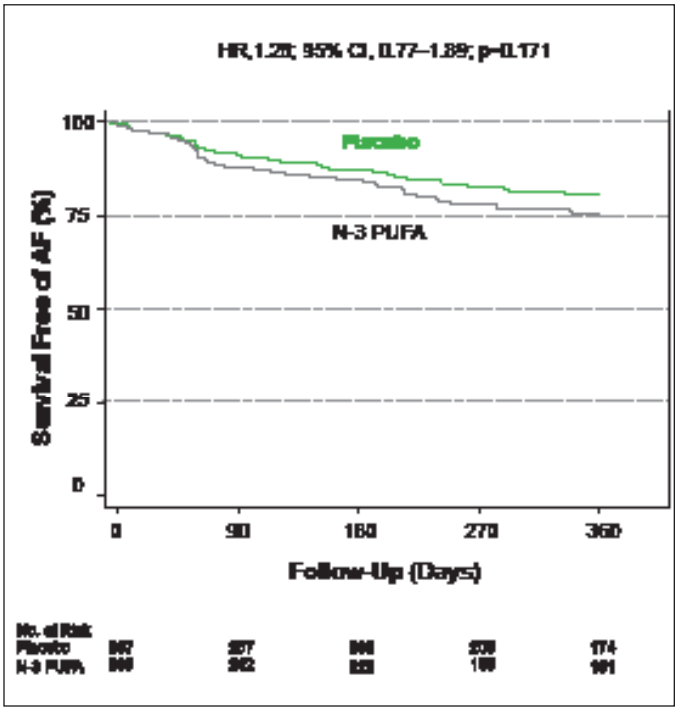
The patient population consisted of men and women at least 21 years of age who had recovered normal sinus rhythm after having been diagnosed in an outpatient setting with symptomatic AF. Patients had either paroxysmal AF (defined as at least 2 symptomatic episodes of documented AF in the previous 6 months 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.

A total of 586 patients received either n-3 PUFA (n=289) or a placebo (n=297). Subjects were mean 66 years of age. Approximately 73% of subjects were enrolled because of single episode of AF that required electrical cardioversion, 63% received amiodarone, 61% received a ß-adrenergic receptor blocking drug, and more than 90% were hypertensive.

After 1 year of follow-up there was no significant difference in the primary efficacy endpoint of survival free of AF between the n-3 PUFA- and placebo-treated patients (HR, 1.28; 95% CI, 0.77 to 1.89; p=0.171; Figure 1), nor were there any significant differences regarding the other prespecified endpoints.

Figure 1. Survival Free of AF.



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According to Dr. Macchia, when the results of this study are added to those of previous studies with a similar hypothesis, the results are clearly neutral, leading to the conclusion that there is no role for n-3 PUFA in the secondary prevention of AF.

Future cardiovascular society guideline updates for the treatment of AF will likely incorporate these findings and note the lack of any benefit for preventing AF recurrence with the tested PUFA regimen and patient population. The benefits (or lack thereof) of other PUFA strategies, including natural sources from fish consumption or use in other patient populations such as lone or new-onset AF, remain unknown.

ASPIRE: Using Aspirin to Prevent Recurrence of VTE

Written by ***Rita Buckley***

Venous thrombosis, which manifests mainly as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common and serious disorder; it occurs in 1 per 1000 individuals per year worldwide, and patients who suffer from DVT or PE are at risk of recurrent events [Rosendaal FR. *PLoS Med* 2012]. There is limited information on safe and effective long-term preventive strategies. Timothy Brighton, MBBS, South Eastern Area Lab Services, Prince of Wales Hospital, Sydney, Australia, presented results from the Aspirin to Prevent Recurrent Venous Thromboembolism [ASPIRE; ACTRN12605000004662] trial.

ASPIRE was a double-blind, randomized, placebo-controlled study that evaluated the efficacy of low-dose aspirin versus placebo in preventing a recurrence of venous thromboembolism (VTE) [Brighton TA et al. *N Engl J Med* 2012]. The primary endpoint was the composite of recurrent symptomatic objectively confirmed DVT, nonfatal PE, or fatal recurrence of VTE.

A total of 822 patients aged ≥18 years were randomized to receive 100 mg/day of aspirin or placebo for up to 4 years following initial anticoagulation therapy. Inclusion criteria were completion of initial anticoagulation therapy after a first unprovoked proximal DVT and/or PE, and commencement of study medication within 6 weeks (and as soon as possible) after the end of initial anticoagulant therapy.

During a median follow-up period of 37.2 months, VTE recurred in 73 of 411 (18%) patients assigned to placebo and in 57 of 411 (14%) assigned to aspirin (6.5% per year vs 4.8% per year; HR aspirin, 0.74; 95% CI, 0.52 to 1.05; p=0.09).

Although there was no significant reduction in the primary endpoint of recurrent VTE, treatment with aspirin was associated with a lower rate of the prespecified secondary broad composite outcomes combing venous and arterial thrombotic events as well as bleeding, including the rate of VTE, myocardial infarction (MI), stroke, or cardiovascular death (HR aspirin, 0.66; 95% CI, 0.48 to 0.92); The rate of VTE, MI, stroke, major bleeding, or death from any cause was reduced by 33% (HR, 0.67; 95% CI, 0.49 to 0.91; p=0.01). There was no significant difference in the rates of major or clinically relevant nonmajor bleeding episodes (0.6%/year with placebo vs 1.1%/year with aspirin; p=0.22) or serious adverse events.

Although the primary hypothesis that aspirin would