### ASPIRIN PRIMARY PREVENTION OF CHD
#### STUDY SYNOPSIS

**Title of Study:** PHYSICIANS' HEALTH STUDY  
**Principal/Investigator(s):** J. MICHAEL GAZIANO, MD, MPH  
**Coordinating Center:** DIVISION OF PREVENTIVE MEDICINE, BRIGHAM AND WOMEN'S HOSPITAL  
**Studied period (years):** 1982-25 Jan 1988  
**(Date of first enrollment):** September 1982  
**(Date of last completed):** April 1984  
**Objectives:** To evaluate if low dose aspirin (325 mg every other day) prevents first MI in apparently healthy male physicians.  
**Methodology:** Double-blind, placebo controlled, randomized trial  
**Number of patients: 22,071 (planned and analyzed)**  
**Study population:** 100 % male 0 % female  
53 Mean age at baseline  
low to moderate Cardiovascular risk at baseline  
**Test products, dose, and mode of administration:** Active aspirin consisted of one 325 mg tablet (as Bufferin, supplied by Bristol-Myers Products) taken every other day.  
**Duration of treatment:** 60.2 months (range 45.8 to 77.0)  
**Criteria for evaluation:**  
**Efficacy:** Endpoints Committee evaluated medical records of self-reported CVD event (stroke, MI, CVD death). Or evaluation of death certificate and associated medical records.  
**Safety:** Endpoints Committee evaluated medical records of self-reported major bleedings. Or evaluation of death certificate.  
**Statistical methods:** Intention-to-treat analysis. Incident events divided by person-years of follow-up. Multiple logistic regression
SUMMARY – CONCLUSIONS
This trial of aspirin for the primary prevention of cardiovascular disease demonstrated a conclusive reduction in the risk of first myocardial infarction. The evidence of stroke and total cardiovascular deaths remained inconclusive because of the inadequate numbers of endpoints.

EFFICACY RESULTS:
On January 25, 1988, the blinded aspirin component was terminated early primarily due to the emergence of a statistically extreme (P < 0.00001) 44% reduction in risk (relative risk 0.56, 95% confidence interval 0.45-0.70, P < 0.00001) of first myocardial infarction in the aspirin group.

SILENT MI INCLUSION OR EXCLUSION RATIONALE:
The study included self-reported myocardial infarctions that were confirmed by an Endpoints Committee based on medical record review.

SAFETY RESULTS:
In the aspirin arm 2979 bleeding events occurred compared to 2248 in the placebo group (relative risk 1.32, 95% confidence interval 1.25-1.40, P < 0.00001). 48 in the aspirin group and 28 in the placebo group needed blood transfusions (relative risk 1.71, 95% CI, 1.09-2.69, P=0.02). One death occurred in the aspirin group due to gastrointestinal hemorrhage; this event was confirmed.

CONCLUSIONS:
This trial of low-dose aspirin in primary prevention of cardiovascular disease in 22,071 apparently healthy US male physicians showed a statistically highly significant 44% reduction in risk of first myocardial infarction.

Protocol and Protocol Amendments: □ Attached

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