

**ASPIRIN PRIMARY PREVENTION OF CHD  
STUDY SYNOPSIS**

Re: Docket 77N-0094

1578 '04 APR 19 10:12

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
Publication (reference): Steering Committee of the Physicians' Health Study Research Group. Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group N Engl J Med 1989;321:129-35. (please attach publication)
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: <u>Efficacy</u> : Endpoints Committee evaluated medical records of self-reported CVD event (stroke, MI, CVD death). Or evaluation of death certificate and associated medical records. <u>Safety</u> : 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

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## STUDY SYNOPSIS

### 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.

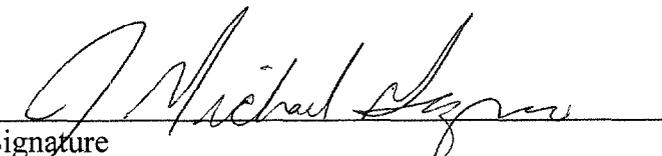
### SAFETY RESULTS:

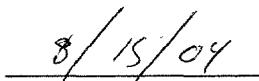
In the aspirin arm 2979 bleeding events occurred compared to 2248 in the placebo group (relative risk 1.32, 95% confidence interval 1.25-1.40,  $P < 0.00001$ ). 48 in the aspirin group and 28 in the placebo group needed blood transfusions (relative risk 1.71, 95% CI, 1.09-2.69,  $P=0.02$ ). One death 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

  
Signature

  
Date

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