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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: The life expectancy of a trial

The original Physicians' Heath Study (PHS) was started in 1980 and was funded by the National Cancer Institute and the National Heart, Lung, and Blood Institute. It was unique in that it was done entirely by mail, including distribution of study treatments and collection of followup information.

Interest in aspirin came in the 1940s when Lawrence Craven, M.D., observed excessive bleeding among children who chewed aspirin gum to ease pain after tonsillectomies. Craven assumed that aspirin somehow prevented blood from clotting, and guessed that aspirin may prevent heart attacks caused by clots in coronary arteries.

Male physicians, aged 40 through 84, registered in the American Medical Association, were mailed invitations to join the PHS. Those willing and eligible were enrolled in a run-in phase of aspirin and placebo beta-carotene.

A total of 22,071 men were randomized in equal numbers to:
aspirin and beta-carotene,
aspirin and beta-carotene placebo,
aspirin placebo and beta-carotene,
and
aspirin and beta-carotene placebos.

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The exclusion of women put the PHS in company with the Multiple Risk Factor Intervention Trial (MRFIT) and Coronary Drug Project (CDP). All three trials were criticized for having excluded women.

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The aspirin component of the trial was stopped in late 1987 because of benefit:
At a special meeting on December 18, 1987, the external Data Monitoring Board of the Physicians' Health Study took the unusual step of recommending the early termination of the randomized aspirin component of the trial, primarily because a statistically extreme beneficial effect on nonfatal and fatal myocardial infarction had been found. Basing its decision on the totality of the evidence, the board recommended that participants be informed of their aspirin treatment assignment and that the findings to date from that component of the trial be reported as soon as possible. (NEJM 318; 262-264, 1988)

The final report of the aspirin component of the PHS published the following year (NEJM 321; 129-35; 1989) stated that:
Further analyses showed that the reduction in the risk of myocardial infarction was apparent only among those who were 50 years of age and older. The benefit was present at all levels of cholesterol, but appeared greatest at low levels. The relative risk of ulcer in the aspirin group was 1.22 (169 in the aspirin group as compared with 138 in the placebo group; 95 percent

confidence interval, 0.98 to 1.53; P = 0.08), and the relative risk of requiring a blood transfusion was 1.71.

The finding that low-dose aspirin decreased the risk of a first myocardial infarction was good news for people at risk of MIs and for Bayer. Before long most everybody I knew at risk of a first MI, including me, was on a daily dose of baby aspirin.

The US Preventative Service Task Force (USPSTF) has issued statements on use of aspirin as a primary prevetative for MI over time, increasingly cautious regarding usage. It was their caution that led me to ditch baby aspirin about 8-10 years ater starting.

The last one (issued 26 April 2022) was most explicit. It recommended against initiating low-dose aspirin for primary prevention of CVD in adults 60 years or older. (JAMA. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983)

So. Back to square one.