Figure 10.5: EXPERIMENTAL PLANS: Meta-Analysis of Aspirin Data

Science **263**(#5143): 24 (1994) [DC Library call number: PER Q1.S35]

META-ANALYSIS

A hearty endorsement for Aspirin

Aspirin is one of the world's most widely used drugs, but a major study being published this week suggests it is not used widely enough. If everybody known to be at high risk of vascular disease were to take half an aspirin a day, about 100,000 deaths and 200,000 nonfatal heart attacks and strokes could be avoided worldwide each year, the study indicates. "This is one of the most cost-effective drug interventions one could have in developed countries," says Oxford University epidemiologist Richard Peto, one of the coordinators of the study, a statistical overview, or meta-analysis, of clinical trials in which aspirin was used to prevent blood clots.

It has long been known that aspirin helps prevent blood clots by blocking one of the enzymes that cause platelets to aggregate, and many studies have shown that the drug can reduce the incidence of heart attacks and strokes. But until now there has been no consensus on which patients should receive such treatment and when. Some studies indicate that aspirin reduces stroke only in men; others have suggested that it does nothing for diabetics; and the rare side-effect of cerebral hemorrhage has led some researchers to argue against its use in vascular disease sufferers who have high blood pressure.

This lack of consensus has led to patchy use of anti-platelet drugs: A 1993 study, for instance, found that only 60% of acute heart attack patients in U.S. academic centers were getting such therapy. Says epidemiologist Charles Hennekens of Harvard Medical School: "We need wider indications for the use of aspirin. We need it in women, in hypertensives ..... We need to get FDA [the U.S. Food and Drug Administration] to act to influence doctors."

The new meta-analysis, which covers both aspirin and more expensive antiplatelet drugs, combined the results of 300 trials involving 140,000 patients. Its recommendation: A regime of half a tablet of aspirin a day is valuable for all victims of heart attack and stroke, and other at-risk patients such as angina sufferers and recipients of coronary bypass grafts (see table). "It's not complicated," says Peto. The full analysis will be published in three consecutive issues of the *British Medical Journal* beginning on 8 January.

While the results are likely to bring consensus to the field, there are still a few areas of uncertainty. One major disagreement surrounds the study's finding that aspirin can reduce thrombosis in patients immobilized by surgery, where some of the studies were not double-blinded, and therefore could be biased. Worried about this possibility, thrombosis expert Anthonie Lensing of Amsterdam's Academic Medical Center and cardiovascular clinicians Jack Hirsch and Mike Gent of McMaster University in Hamilton, Ontario, have reanalyzed a smaller set of data. They included only results of trials that had faultless methodology and looked separately at patients in general surgery and those who had had procedures such as hip replacements, where the surgery itself can damage veins in the leg and further increase the risk of thrombosis. Their conclusion: Aspirin is beneficial only following orthopedic surgery.

Oxford cardiologist Rory Collins, another coordinator of the study, counters that splitting the data into such small chunks defeats the object of conducting a meta-analysis of many trials. And he notes that if the data for general and orthopedic surgery are considered together, there is still a significant benefit from aspirin, even if methodologically suspect trials are excluded.

Another key question, which the overview does not claim to answer, is whether generally healthy people should take aspirin to prevent vascular disease. But the answer may not be too long in coming: 40,000 U.S. female health care workers are now involved in a trial to test the effectiveness of aspirin in the primary prevention of vascular disease.

Peto stresses, however, that such future concerns should not deflect attention from the urgent need for wider use of aspirin now among people at high risk of vascular disease. Collins, Peto, and Hennekens have already urged the FDA to extend its guidelines on the use of aspirin against vascular disease. The FDA currently recommends anti-platelet therapy only for sufferers of unstable angina, as a measure to reduce secondary heart attacks after an initial coronary, and to reduce secondary strokes in men, but not women. Concludes Peto: "It's time for doctors to look at this evidence and really change their practice."

– **Peter Aldhous**

SUMMARY OF RESULTS OF ASPIRIN TRIALS			Proportion who suffered nonfatal stroke, nonfatal heart attack, or death during the trial.	
Type of patient	**Length of treatment**	**Number of patients**	**Treatment group**	**Control group**
Suspected acute heart attack	1 month	20,000	10%	14%
Previous history of heart attack	2 years	20,000	13%	17%
Previous history of stroke	3 years	10,000	18%	22%
Other vascular diseases	1 year	20,000	7%	9%

REFERENCES: Antiplatelet Trialists' Collaboration: Collaborative overview of randomized trials of antiplatelet therapy – I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *Brit. Med. J.* **308**(#6921): 81-106 (1994). II: Maintenance of vascular graft or arterial patency by antiplatelet therapy. **308**(#6922): 159-168 (1994). III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. **308**(#6923): 235-246 (1994). [DC Library call number: PER R31.B93]

Blank page