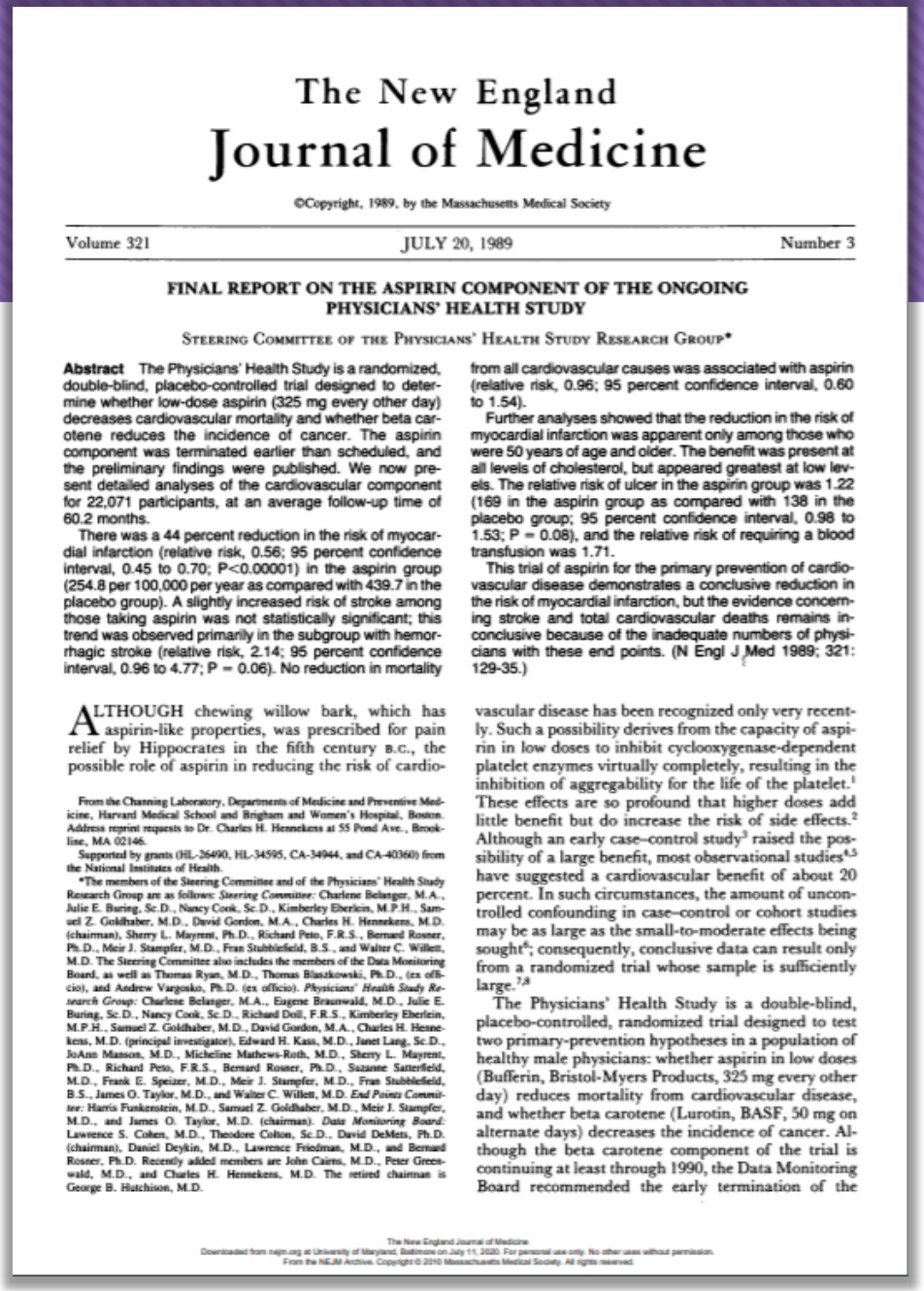
Scenario

A 60 year Native American woman presents to her vascular surgeon with some mild claudication. Her surgeon explains some life style modifications she can make, and suggests that she starts taking daily ASA 325 mg. The patient responds, “I don’t know doc, I really don’t like taking medication—are you sure this will help me?” The doctor responds, that are decades of literature showing that aspirin decreases cardiovascular mortality.

Is that the whole story?

Representation



The New England
Journal of Medicine

Volume 321 JULY 20, 1989 Number 3

FINAL REPORT ON THE ASPIRIN COMPONENT OF THE ONGOING PHYSICIANS' HEALTH STUDY

STEERING COMMITTEE OF THE PHYSICIANS' HEALTH STUDY RESEARCH GROUP*

Abstract The Physicians' Health Study is a randomized, double-blind, placebo-controlled trial designed to determine whether low-dose aspirin (325 mg every other day) decreases cardiovascular mortality and whether beta carotene reduces the incidence of cancer. The aspirin component was terminated earlier than scheduled, and the preliminary findings were published. We now present detailed analyses of the cardiovascular component for 22,071 participants, at an average follow-up time of 60.2 months.

There was a 44 percent reduction in the risk of myocardial infarction (relative risk, 0.56; 95 percent confidence interval, 0.45 to 0.70; P<0.00001) in the aspirin group (254.8 per 100,000 per year as compared with 439.7 in the placebo group). A slightly increased risk of stroke among those taking aspirin was not statistically significant; this trend was observed primarily in the subgroup with hemorrhagic stroke (relative risk, 2.14; 95 percent confidence interval, 0.96 to 4.77; P = 0.06). No reduction in mortality from all cardiovascular causes was associated with aspirin (relative risk, 0.96; 95 percent confidence interval, 0.60 to 1.54).

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.

This trial of aspirin for the primary prevention of cardiovascular disease demonstrates a conclusive reduction in the risk of myocardial infarction, but the evidence concerning stroke and total cardiovascular deaths remains inconclusive because of the inadequate numbers of physicians with these end points. (N Engl J Med 1989; 321: 129-35.)

ALTHOUGH chewing willow bark, which has aspirin-like properties, was prescribed for pain relief by Hippocrates in the fifth century B.C., the possible role of aspirin in reducing the risk of cardiovascular disease has been recognized only very recently. Such a possibility derives from the capacity of aspirin in low doses to inhibit cyclooxygenase-dependent platelet enzymes virtually completely, resulting in the inhibition of aggregability for the life of the platelet.[1] These effects are so profound that higher doses add little benefit but do increase the risk of side effects.[2] Although an early case–control study[3] raised the possibility of a large benefit, most observational studies[4,5] have suggested a cardiovascular benefit of about 20 percent. In such circumstances, the amount of uncontrolled confounding in case–control or cohort studies may be as large as the small-to-moderate effects being sought[6]; consequently, conclusive data can result only from a randomized trial whose sample is sufficiently large.[7,8]

The Physicians' Health Study is a double-blind, placebo-controlled, randomized trial designed to test two primary-prevention hypotheses in a population of healthy male physicians: whether aspirin in low doses (Bufferin, Bristol-Myers Products, 325 mg every other day) reduces mortality from cardiovascular disease, and whether beta carotene (Lurotin, BASF, 50 mg on alternate days) decreases the incidence of cancer. Although the beta carotene component of the trial is continuing at least through 1990, the Data Monitoring Board recommended the early termination of the

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Supported by grants (HL-26490, HL-34595, CA-34944, and CA-40360) from the National Institutes of Health.

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- Top Tier Journal
- Large Cohort
- Excellent Compliance
- 5 year follow up
- Clinically Relevant endpoint

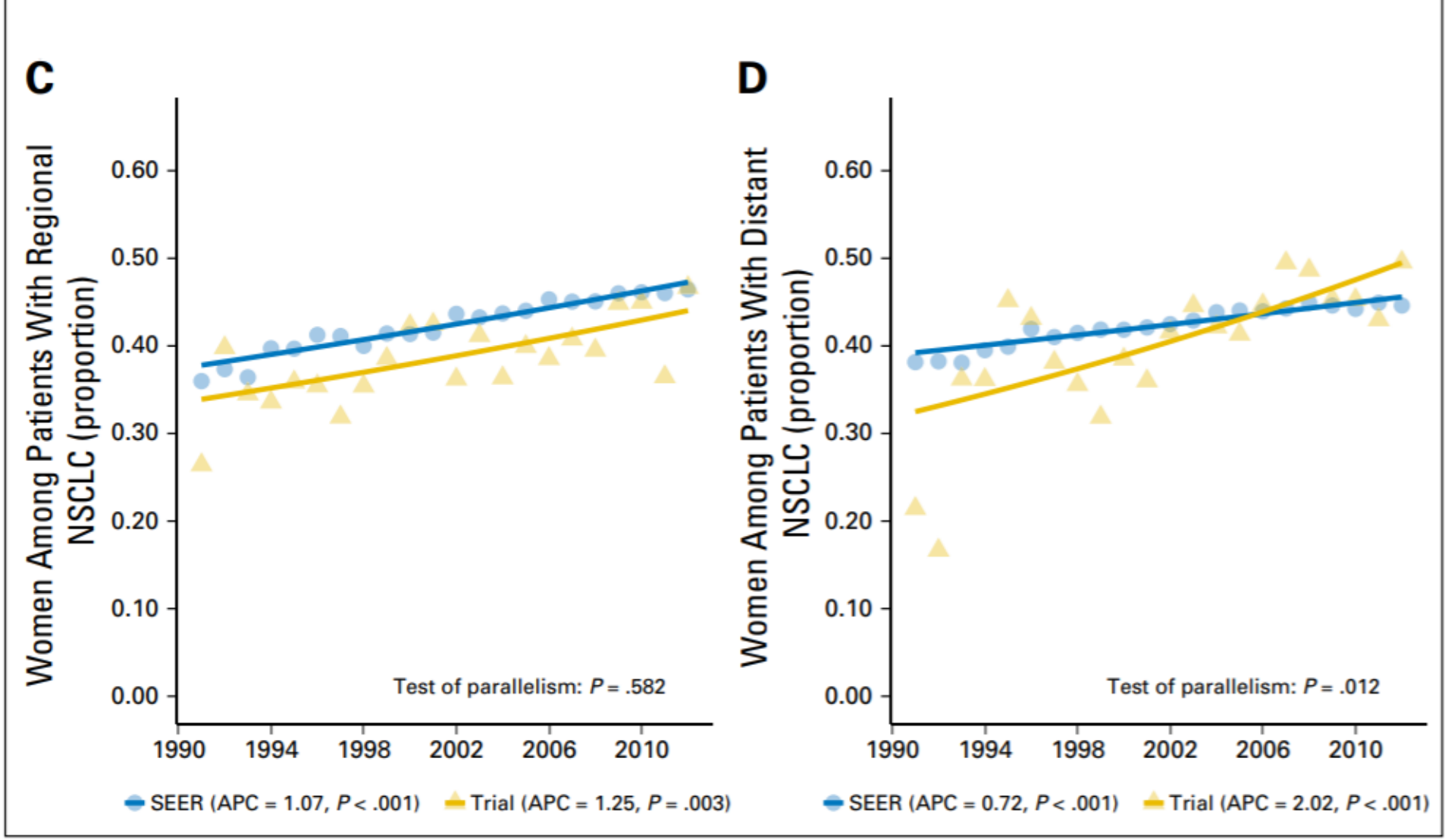
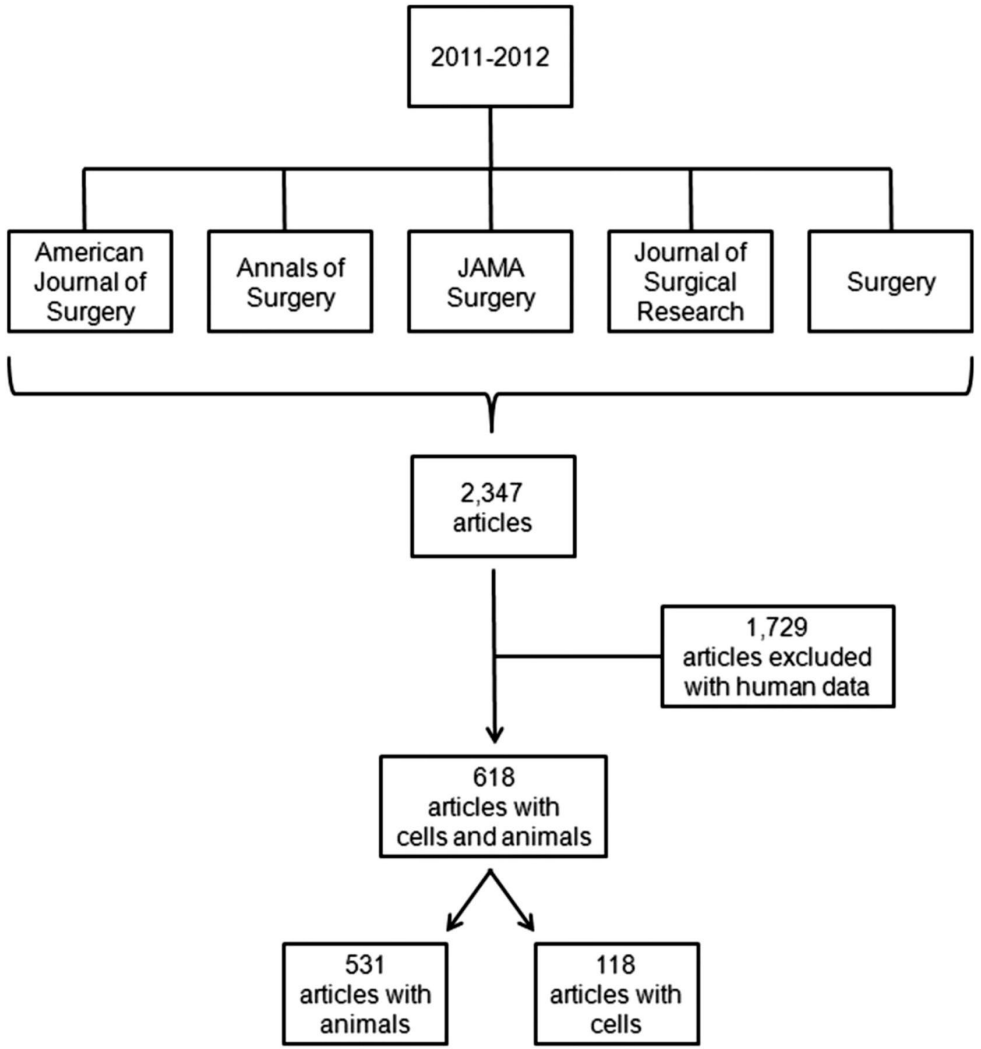
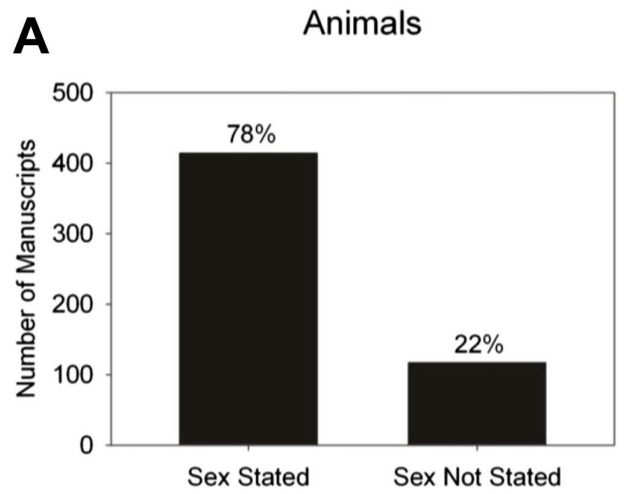


Fig 4. Proportion of elderly and women patients: trial participants and US population, 1990 to 2012. (A) Elderly among patients with regional non–small-cell lung cancer (NSCLC). (B) Elderly among patients with distant NSCLC. (C) Women among patients with regional NSCLC. (D) Women among patients with distant NSCLC. The annual percentage change (APC) *P* value corresponds to testing whether the APC is different from 0. The solid lines represent the fitted values of the joinpoint regression. The year 1990 was excluded from analysis because of the small number of trial participants with regional or distant NSCLC.


2011-2012
American Journal of Surgery
Annals of Surgery
JAMA Surgery
Journal of Surgical Research
Surgery
2,347 articles
1,729 articles excluded with human data
618 articles with cells and animals
531 articles with animals
118 articles with cells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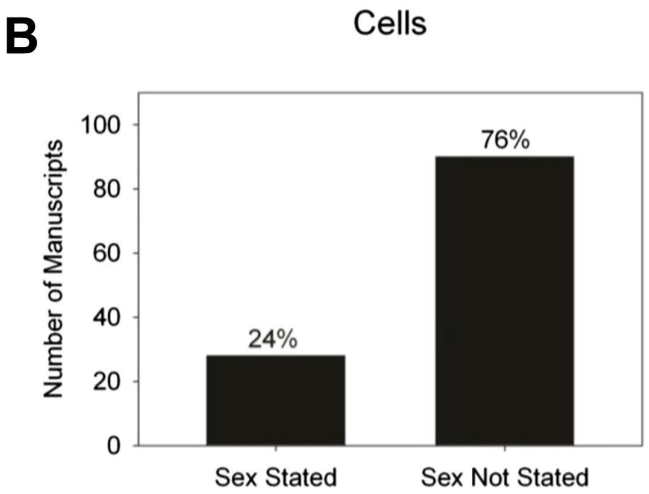
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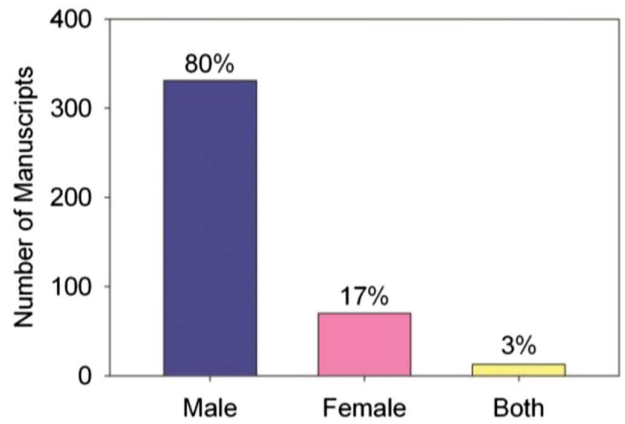
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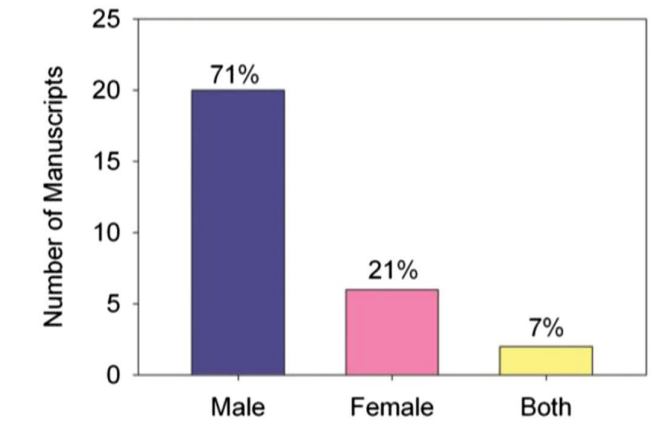
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Too Low a Bar

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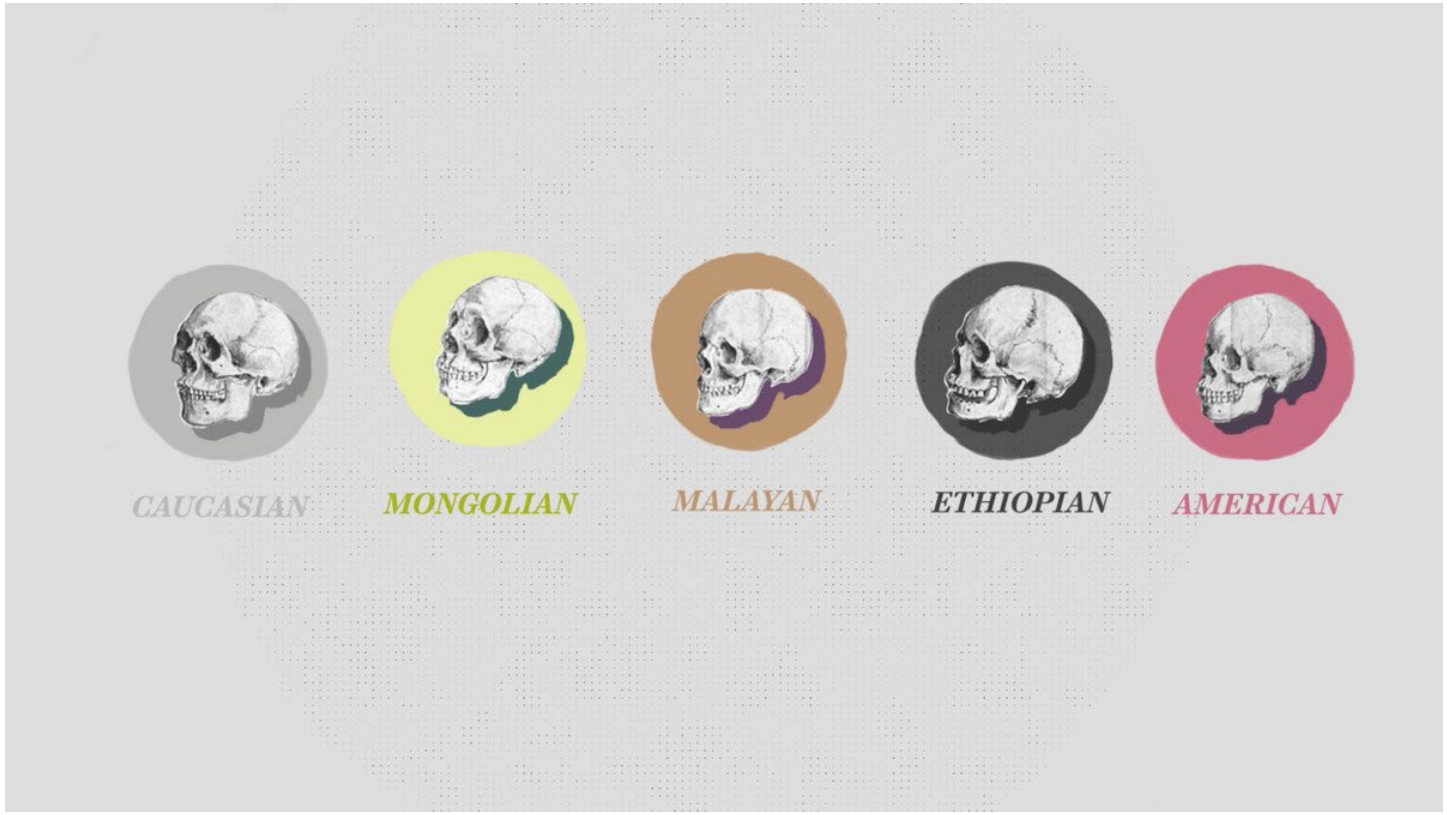

Critiquing the data

Operationalizing

Case Study 1

A 60 year Native American woman presents to her vascular surgeon with some mild claudication. Her surgeon explains some life style modifications she can make, and suggests that she starts taking daily ASA 325 mg. The patient responds, "I don't know doc, I really don't like taking medication—are you sure this will help me?" The doctor responds, that are decades of literature showing that aspirin decreases cardiovascular mortality.

Is that the whole story?

Survey

Please complete the following brief survey to assess your learning from today's session and provide feedback on your experience.