For some of the following studies...¹...

- How was contrast formed?
 - Experimentally
 - * Variants
 - Non-experimentally
 - * Natural/Quasi experiments
 - * Other
- Parameter involved in the contrast..
 - Level (mean) or change in level
 - Proportion:- simple, or product over (discrete) time
 - Rate (Incidence Density)
 - Cumulative Incidence

The James Lind Library

Illustrating the development of fair tests of treatments in health care

http://www.jameslindlibrary.org

The James Lind Library has been created to help people understand fair tests of treatments in health care by illustrating how fair tests have developed over the centuries. At the core of the James Lind Library are key passages and images from books and journal articles, and essays explaining the principles of fair tests. Much of the core is accompanied by commentaries, biographies, portraits, and other relevant material.

Examples - In no particular order

- Do women perform differently on math tests depending on whether they believe math-related gender differences are determined by genetic or social differences? [Applications]
- What causes Sudden Infant Death Syndrome?
- Exposure to Soy-Based Formula in Infancy: Over the years soy-based formulae have been criticised because of concerns that the phyto oestrogens in them might affect the reproductive capacity of infants. [c607 Chapter 8]

- Mild perioperative hypothermia (approximately 2C below the normal core body temperature) is common in colon surgery. We tested the hypothesis that hypothermia both increases susceptibility to surgical-wound infection and lengthens hospitalization. [c607 Chapter 7/8]
- Does sunscreen prevent skin cancer? [c607 Chapter 7]
- The "Mozart Effect" and Enhanced Intelligence: will listening to Mozart improve your reasoning skills? [See also: Science 6 August 1999: Vol. 285. no. 5429, p. 827] [c607 Chapter 7]
- Charles Darwin (1809-1882) hypothesized that cross-fertilized plants produced taller offspring than self-fertilized plants.
- Francis Galton (1822-1911) had seven sets of sweet pea seeds labeled K to Q and in each packet the seeds were of the same weight. He chose sweet peas on the advice of his cousin Charles Darwin and the botanist Joseph Dalton Hooker as sweet peas tend not to self fertilise and the seed weight varies little with humidity. He distributed these packets to a group of friends throughout Great Britain who planted them. At the end of the growing season the plants were uprooted and returned to Galton. He found that "When parents are taller than mediocrity (i.e. the median), their children tend to be shorter than they" and "when parents are shorter than mediocrity (the mean)".

In additional work he investigated geniuses in various fields and noted that their children, while typically gifted, were almost invariably closer to the average than their exceptional parents. He later described the same effect more numerically by comparing fathers' heights to their sons' heights. Again, the heights of sons both of unusually tall fathers and of unusually short fathers was typically closer to the mean height than their fathers' heights.

- Do bed nets treated with insecticide save the lives of children living in sub-Saharan Africa? BMJ 2007;335:639 (29 September), doi:10.1136/bmj.335.7621.639-b
- Does giving extra milk to schoolchildren help them grow more? [cf. Student. The Lanarkshire Milk Experiment. Biometrika, Vol. 23, No. 3/4 (Dec., 1931), pp. 398-406; and Two controlled trials of supplementary feeding of British school children in the 1920s J. R. Soc. Med., Vol. 99, Issue 6, 323-327, June 1, 2006].
- "Over thirty years ago, at several widely scattered places in the world, it was noticed that relatively small groups of people had a significantly

 $¹_{\rm jh~Jan~05,~2015}$

- Studies on the nicotine exposure of individual smokers: Changes in mouth-level exposure to nicotine on switching to lower nicotine cigarettes. [Int J Addict. 1976;11(6):933-50.]
- Optimal Vehicle Speed for Maximum Fuel economy:- Optimal efficiency can be expected while cruising with no stops, at minimal throttle and with the transmission in the highest gear. For most cars these conditions are satisfied at a speed of approximately xx Km per hour. en.wikipedia.org/wiki/Fuel_economy-maximizing_behaviors
- Workers in modern office buildings frequently have unexplained workrelated symptoms or combinations of symptoms. We assessed whether ultraviolet germicidal irradiation (UVGI) of drip pans and cooling coils within ventilation systems of office buildings would reduce microbial contamination, and thus occupants' work-related symptoms. [D Menzies, Lancet]
- The sick building syndrome is the term given to a constellation of symptoms reported by workers in modern office buildings, hypothesized to occur when the supply of outdoor air is reduced, because of the accumulation of contaminants arising from within the building. We undertook this study to determine the effect of changing the supply of outdoor air in office buildings on the symptoms reported by workers and their perception of the indoor environment. [D Menzies, NEJM]
- Because of a belief that the use of cellular telephones while driving may cause collisions, several countries have restricted their use in motor vehicles, and others are considering such regulations. We studied whether

using a cellular telephone while driving increases the risk of a motor vehicle collision. [D Redelmeier, NEJM]

- Longer term effects of New York State's law on drivers' handheld cell phone use: a study to determine whether substantial short term declines in drivers' use of handheld cell phones, after a state ban, were sustained one year later. [McCartt AT, Geary LL. Inj Prev. 2004 Feb;10(1):11-5.] Longer-term effects of Washington, DC, law on drivers' hand-held cell phone use: a study to determine whether the substantial short-term declines in drivers' use of hand-held phones achieved in the District of Columbia (DC) were sustained 1 year after a ban. [McCartt AT, Hellinga LA. Traffic Inj Prev. 2007 Jun;8(2):199-204.]
- Do speeding tickets reduce the likelihood of receiving subsequent speeding tickets? Speeding tickets are the most commonly used tool to deter speeders, yet little is known about how speeding citations affect individual drivers' behavior over time. [Lawpoolsri S, Li J, Braver ER. Traffic Inj Prev. 2007 Mar;8(1):26-34]
- Differences in proximal femur bone density over two centuries: The incidence of osteoporotic hip fractures in Northern Europe has been increasing over the past few decades faster than the rate adjusted for increased life expectancy. One important factor that determines osteoporotic fracture risk is bone density. The (...) gave us the opportunity to compare the rate of bone loss in the femora of women from two centuries ago with that of present-day women. [Lees B et al. Lancet 1993; 341: 673-75]. [c678]
- Does using a Macintosh lead to sloppier writing? Quill or Computer?

Story in Los Angeles Times, August 9, 1990. [c607 Chapter 2]

[This was before Windows, when PC users had to use a command-line—non-graphical—DOS interface]

Using an Apple Macintosh can lead to "sloppier writing and fluffier topics," according to research by a University of Delaware writing instructor. Analysis of a random sample found that 30% of the Mac writers used complex sentences compared to 50% of the IBM-clone writers.

Sentence length averaged 16.3 words for the Mac essays and 22.6 from those written on PCs. And the Kincaid Scale, a measure of readability, showed Mac users writing at the 8th grade level versus 12th grade for the IBM clone group.

"Never before in 12 years of teaching had I seen such a sloppy bunch of papers," wrote Delaware's Marcia Peoples Halio in "Student Writing:

Can the Machine Maim the Message?" "Words were misspelled; commas were placed haphazardly; semicolons were virtually non- existent or placed by means of "breath" punctuation rules, and such fine points as quotation marks, apostrophes and question marks were treated with gay abandon." The Mac's format seems to "encourage a simple sentency structure and childish vocabulary. On the other hand, the papers that the Mac class turned in were often very creatively illustrated."

Halio, Marcia P. "Student Writing: Can the Machine Maim the Message?" Academic Computing 4 (1990a): 16-19.

Title: Computers and Student Writing: Maiming the Macintosh (A Response). Authors: Youra, Steven Source: Computers and Composition, v7 n3 p81-88 Aug 1990 Abstract: Argues that Marcia Peoples Halio's "Student Writing: Can the Machine Maim the Message?" (which argues that students using IBM computers wrote better than those using Macintosh computers) is flawed by poor experimental design and is filled with questionable logic and evidence. Contends that she overlooks many specific features that make Macintoshes a valuable tool. (RS)

ERIC: EJ414703 Title: Maiming Re-Viewed. Authors: Halio, Marcia Peoples Source: Computers and Composition, v7 n3 p103-07 Aug 1990 Publication Date: 1990-00-00 Abstract: Responds to criticisms of "Student Writing: Can the Machine Maim the Message?." Argues that cognitive psychologists, human computer interaction specialists, and teachers have provided "heavy support." Supports the use of "Writer's Workbench," the writing topic selection, self-selection, teaching methods, computer training, qualitative judgments about writing, and the research design of the original article. (RS)

- To determine the effect of helmets on the risk of head and neck injuries in skiers and snowboarders. [Hagel BE, Pless IB, Goulet C, Platt RW, Robitaille Y. BMJ. 2005 Feb 5;330(7486):281. Epub 2005 Jan 4.]
- Do Speed Limits Reduce Traffic Accidents? [Applications... Statistics: A Guide to the Unknown]
- The Salk Polio Vaccine in 1954: Safe? Effective? Potent?

March of Dimes Video: 1 http://www.umich.edu/news/Vid/MoD2.ram

March of Dimes Video: 2 http://www.umich.edu/news/Vid/MoD1.ram

Press Conference April 1955 http://www.umich.edu/news/Vid/newsconf.ram

Michigan 50th Anniversary: http://www.polio.umich.edu/

http://umtv-live.rs.itd.umich.edu/mc/ccook.ram

Michigan 50th Anniversary Video Links: http://www.polio.umich.edu/history/video.html

- Does Aspirin Prevent Myocardial Infarction and Stroke?
- Probit Study
- De-horning Rhinos
- Oatmeal as a cholesterol; lowering agent?
- Treatments for Prostate Cancer
- Hearing loss portable music players
- Vitamin D
- HPV vaccine
- Folate [Applications]
- Male circumcision for HIV prevention in men in Africa
- Does the "6 pack" encourage women to stop breastfeeding?
- Does supplementation in the newborn nursery encourage women to stop breastfeeding? [Gray-Donald]
- Lifespan and testosterone: Coronary heart disease and atherosclerosis are the most frequent causes of death among men. Because these conditions occur more frequently in men than in women, it is often assumed that androgens play a causative role. Indeed, correlations between circulating testosterone levels and coronary heart disease have been made, as have negative correlations between blood lipids and androgens, in particular between high density lipoprotein cholesterol and testosterone. This hypothesis that testosterone may contribute to men's shorter lifespan is difficult to prove experimentally, not least because ethical considerations preclude many obvious tests. But (...) should provide information on the influence of testosterone on longevity...

Scientific Correspondence Nature Vol 366, 18 Nov 1993, page 215

- Antibiotic disruption of the normal intestinal flora is a well-known risk factor for Clostridium difficile-associated di- arrhea. Reduced gastric acidity has been suggested as a risk factor, and we hypothesized that proton pump inhibitors, be- cause of their potency, may be an independent risk factor for this problem. [CMAJ July 6, 2004; 171 (1) Online-1. Fast-tracked article. Early release, published at www.cmaj.ca on June 4, 2004. Subject to revision.]
- Garlic as an Insect Repellent

To the Editor: Lyme borreliosis is the most common vector-borne disease in Sweden, and as many as 10000 individuals are thought to be affected each year. Recent studies have suggested that individual variability in vector attachment may be linked to different body odors. Other studies suggested that diethyltoluamide is the best repellent against insect vectors and permethrin against ticks, in particular. However, insect repellents may have adverse effects on humans and animals. Because military personnel are at particularly high risk for tick bites and tick-borne diseases, we conducted a (...) of garlic (Allium sativum) to prevent tick bites among Swedish marines. [Louise Stjernberg, Letter (Reprinted) JAMA, August 16, 2000Vol 284, No. 7 831]

- Impact of a helmet law on two wheel motor vehicle crash mortality [c626]
- Insufficient Sleep and Traffic Accidents

To the Editor: It has become increasingly clear that insufficient sleep and disrupted circadian rhythms are a major public health problem. For instance, in 1988 the cost of sleep related accidents [in the USA we presume] exceeded \$56 billion and included 24,318 deaths and 2,474,430 disabling injuries. Major disasters, including the nuclear accident at Chernobyl, the Exxon Valdez oil spill, and the destruction of the space shuttle Challenger, have been linked to insufficient sleep, disrupted circadian rhythms, or both on the part of involved supervisors and staff. It has been suggested that as a society we are chronically sleep deprived and that small additional losses of sleep may have consequences for public and individual safety.

We can use noninvasive techniques [Canadian data] to examine the effects of minor disruptions of circadian rhythms on normal activities if we take advantage of (...)

Stanley Coren (UBC). N Engl J Med. 1996 Apr 4;334(14):924.

See also correspondence on Aug 1, 1996 and the letter by A. Vincent A, N Engl J Med. 1998 Oct 15;339(16):1167-8.

See also Varughese J, Allen RP. Sleep Med. 2001 Jan;2(1):31-36 and Hicks GJ, Davis JW, Hicks RA. Percept Mot Skills. 1998 Jun;86(3 Pt 1):879-82, for two American studies, and Lambe M, Cummings P. Accid Anal Prev. 2000 Jul;32(4):609-11 for a Swedish study.

- Sleep Medical Residents
 - Feddock CA, Do pressure and fatigue influence resident job performance? Med Teach. 2007 Jun;29(5):495-7.
 - Arora VM Improving sleep hygiene of medical interns: can the sleep, alertness, and fatigue education in residency program help? Arch Intern Med. 2007 Sep 10;167(16):1738-44.
 - Barger LK Impact of extended-duration shifts on medical errors, adverse events, and attentional failures. PLoS Med. 2006 Dec;3(12):e487.
 - Surani S Sleepiness in medical residents: impact of mandated reduction in work hours. Sleep Med. 2007 Jan;8(1):90-3. Epub 2006 Dec 6.
 - Landrigan CP Interns' compliance with accreditation council for graduate medical education work-hour limits. JAMA. 2006 Sep 6;296(9):1063-70.
 - Ayas NT Extended work duration and the risk of self-reported percutaneous injuries in interns. JAMA. 2006 Sep 6;296(9):1055-62.
 - Arora V The effects of on-duty napping on intern sleep time and fatigue. Ann Intern Med. 2006 Jun 6;144(11):792-8. Summary for patients in: Ann Intern Med. 2006 Jun 6;144(11):I20.
 - Rosen IM Evolution of sleep quantity, sleep deprivation, mood disturbances, empathy, and burnout among interns. Acad Med. 2006 Jan;81(1):82-5.
 - Barger LK Extended work shifts and the risk of motor vehicle crashes among interns. N Engl J Med. 2005 Jan 13;352(2):125-34.
 - Landrigan CP Effect of reducing interns' work hours on serious medical errors in intensive care units. N Engl J Med. 2004 Oct 28;351(18):1838-48.
 - Lockley SW Effect of reducing interns' weekly work hours on sleep and attentional failures. N Engl J Med. 2004 Oct 28;351(18):1829-37.
 - Papp KK The effects of sleep loss and fatigue on resident-physicians: a multi-institutional, mixed-method study. Acad Med. 2004 May;79(5):394-406.

- Rollinson DC The effects of consecutive night shifts on neuropsychological performance of interns in the emergency department: a pilot study. Ann Emerg Med. 2003 Mar;41(3):400-6.
- Women are Safer Pilots: Study

LONDON- Initial results of a study by Britain's Civil Aviation Authority shows that women behind the controls of a plane might be safer than men. The study shows that male pilots in general aviation arc more likely to have accidents than female pilots. Only 6 per cent of Britain's general aviation pilots are women. According to the aviation magazine Flight International, there have been 138 fatal accidents in general aviation in the last 10 years, and only two involved women - less than 1.5 per cent of the total. [Woman News, page F1 The Montreal Gazette, August 21st, 1995]

• Does reducing speed limits on toll roads lead to reductions in the rate of crashes and injuries?

Changes, following a 5-15 mph (8-24 kph) decrease in speed limits on the Illinois Tollway

[Doege TC, Levy PS. Am J Epidemiol. 1976 Feb;103(2):236-41 - c626]

- Mazer
- Fortification of Foods with Folic Acid: Inpact on Neural Tube Defects [USA/Canada c626]
- Effects of screening on cervical cancer incidence and mortality in New South Wales implied by influences of period of diagnosis and birth cohort
- Effect of air-pollution control on death rates in Dublin, Ireland: an intervention study
- A matter of life and death: population mortality and football results
- Birth order and mortality: a life-long follow-up of 14,200 boys and girls born in early 20th century Sweden
- Pour battre (Patrick) Roy, mieux vaut lancer bas... [La Presse, avril 1994]
- The role of stimulation in the delay of onset of crying in the newborn infant.

[T. Gordon and B. M. Foss Quarterly J of Experimental Psychol., 18, 79-81. 1966]

Crying is said to result from stimulus need. An experiment was done in which infants were stimulated during quiet periods to see if this would postpone the onset of crying. The results were positive. An alternative explanation in terms of internal temperature control is considered.

Crying in the human infant has been treated either (1) as a reaction to an unpleasant external stimulus or (2) as a response to an internal need. Point (1) is illustrated by Skinner's observation (1959, p. 420) that he was able to reduce the amount of crying of his own child by keeping it in a compartment in which the temperature was held constant and the child could move about without the constraints of clothing. Point (2) is illustrated by the terms "stimulus need" and "stimulus hunger' which have been used by investigators who are concerned with the kind of stimulation required for normal development in both humans and animals (Thompson, 1955, p. 133). Presumably the infant requires varied stimulation, the kind and quantity of which changes as the child grows. Crying can be regarded as an index of the absence of such stimulation.

Crying occurs fairly regularly in the human infant before feeding. It also occurs, though less frequently, when there is no obvious indication of discomfort: the child need not be windy, wet or in discernible pain. In the newborn infant, one of the first efforts which the mother makes to stop the infant from crying is to rock it. Sometimes this is successful and the infant drops off to sleep again. By analog with hunger, the need involved is reduced. If it is not other efforts will be made to find out why the baby is crying and how to stop it.

Since rocking seems an effective means of stopping the baby from crying when it is not hungry or in pain, it would appear to answer to some of the stimulus needs of the young infant. If it can be effective in stopping the infant from crying, rocking the child before it cries should prevent or delay the infant's crying effectively. That is to say, if crying can result from stimulus hunger then appropriate stimulation should put off the onset of crying. The following experiment was done to test this hypothesis.

• The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type

To evaluate the relation between elective cesarean section and vertical transmission of human immunodeficiency virus type 1 (HIV-1), we performed a meta-analysis using data on individual patients from 15 xxxxxxxx xxxxx studies. [The International Perinatal HIV Group. N Engl J Med. 1999 Apr 1;340(13):977-87.]

• The Risk of Human Immunodeficiency Virus-1 Infection in Twin Pairs

Born to Infected Mothers in Africa [Biggar R J850 The Journal of Infectious Diseases: 2003:188 (15 September]

• High risk of HIV-1 infection for first-born twins. The International Registry of HIV-exposed Twins.

To examine the epidemiology and natural history of mother-to-infant transmission of human immunodeficiency virus type 1 (HIV-1), especially genetic and intrapartum exposure factors, we obtained data on twins and triplets born to women infected with the virus. 40 investigators in nine countries contributed demographic, clinical, and epidemiological data on 100 sets of twins and 1 set of triplets. Among the 66 evaluable sets, HIV-1 infection was more common in first-born than in second-born twins (p = 0.004). In 22 sets, only one twin was infected (18 first-born, 4 secondborn). 50% of first-born twins delivered vaginally and 38% of first-born twins delivered by caesarean were infected, compared with 19% of secondborn twins delivered by either route. HIV-1 infection status tended to be concordant in more monozygotic (14 of 17 sets) than dizygotic (26 of 43) sets, but the frequency and clinical signs of HIV-1-related disease were similar in only 3 of the 10 sets with both children infected. These findings suggest that some infants may be infected in utero before labour but that a substantial proportion of HIV-1 transmission occurs as the first twin encounters the cervix and birth canal. Such measures as cleansing of the birth canal and caesarean delivery before membrane rupture might reduce the risk of transmission for infants born to HIV-1-infected women and should be the subjects of controlled clinical trials. Caesarean section should not be regarded as a wholly preventive measure, however, since substantial proportions of both first-born and second-born twins delivered in this way were infected.

[Goedert JJ, Dulige AM, Amos CI, Felton S, Biggar RJ. Lancet. 1991 Dec 14;338(8781):1471-5. Comment in: Lancet. 1992 Mar 7;339(8793):628.]

• Psychological Stress and Susceptibility to the Common Cold

It is commonly believed that life stressors increase susceptibility to infectious disease... When demands imposed by events exceed ability to cope, a psychological stress response is elicited (ref.). This response is composed of negative cognitive and emotional states. In turn, these states are thought to alter immune function through autonomic nerves that connect the central nervous system to immune tissue ...

[Cohen S et al. New Eng J of Med 1991; 325:606-612.]

• The Lidkping Accident Prevention Programme–a community approach to preventing childhood injuries in Sweden.

In Sweden about 100 children 0-14 years die from accidental injuries every year, roughly 40 girls and 60 boys. To reduce this burden the Safe Community concept was developed in Falkping, Sweden in 1975. Several years later a second programme was initiated in Lidkping. The objectives of this paper are to describe the programme in Lidkping and to relate it to changes in injury occurrence.

[Svanstrm L, Ekman R, Schelp L, Lindstrm A. Inj Prev. 1995 Sep;1(3):169-72. Comment in: Inj Prev. 1996 Jun;2(2):131-3; discussion 133-4]

• The lacing defence: (...) study of thresholds for detecting addition of ethanol to drinks

In Britain it is a criminal offence to drive if the driver's measured ethanol concentration exceeds 35 micrograms per 100 ml in breath or 80 mg per 100 ml in blood. Those found guilty are disqualified from driving unless they can give a special reason why this should not happen. Most commonly, a defendant claims a friend has *jilacedic* a drink by adding spirits, so that he or she has unwittingly consumed an amount of ethanol sufficient to raise the blood ethanol concentration above the limit. Doctors are sometimes asked in court whether a defendant would have known that a drink has been laced. We conducted (...) to discover whether volunteers were able to tell that vodka had been added to a drink ...

[N J Langford, T Marshall, R E Ferner BMJ 1999;319:1610-1610, 18 December]

• Sexual activity and the lifespan of male fruitflies

A cost of increased reproduction in terms of reduced longevity has been shown for female fruitflies, but not for males.

Linda Partridge and Marion Farquhar. Nature, 294, 580-581, 1981.

• The Heritability of Otitis Media

Anatomical, physiological, and epidemiological data indicate that there may be a significant genetic component to prolonged time with and recurrent episodes of otitis media in children.

Objective: To determine the genetic component of time with, and episodes of, middle ear effusion and acute otitis media during the first 2 years of life.

[E M. Mandel, P A. Fall, H E. Rockette. JAMA. 1999;282:2125-2130]

• Effects of sulfuric acid aerosol on pulmonary function in human subjects: an environmental chamber study.

Sulfuric acid (H2SO4) aerosol is an air pollutant formed from oxidation of atmospheric sulfur dioxide, with subsequent hydration. A more recent source of H2SO4 is the automobile catalytic converter. Sulfuric acid is a more toxic pollutant than SO2, and has been suggested as one of the irritants contributing to to the excess mortality and morbidity resulting from the London smog of 1962, where excessively high levels were presumed to occur (Lawther, 1963). In 1976, it was estimated that the peak U.S. urban atmospheric burden of H2SO4 was 20 micrograms/cubic meter;; however, it is anticipated that with increased use of high-sulfur fuel, and more widespread use of catalytic converter-equipped automobiles, the level could rise three- or fourfold.

Animal studies (Amdur, 1958; Alarie et al., 1973, 1975) have revealed adverse pulmonary function effects to extremely high levels of H2S04 aerosol (> 2000 ug/m3).

Amdur et al. (1952) reported adverse effects (decreased flow rates) in human subjects exposed by face mask to high concentrations of H2SO4 mist (350-500 ,ug/m3 of l-um particle size for 5-15 min). Sim and Pattle (1957) reported symptoms of respiratory tract irritation and increased airway resistance in human subjects exposed to high concentrations of H2SO4 acid mist (> 3000,ug/m3 of l-um particle size for 10 min) in high humidity (90% RH).

More recently, Avol et al. (1979) reported no effects on pulmonary function following exposure to 1OO ug/m3 H2SO4 for 2 hr, and Sackner et al. (1978) found no effects following exposure of normal and asthmatic humans to 100 and 1000 um/m3 for 10 min. Utell et al. (1979) did find significant changes in flow rates and increased bronchial reactivity, following exposure to 1000 ug/m3 H2SO4 aerosol for 16 min.

The purpose of this investigation was to determine if exposure of human subjects to levels of H2SO4 aerosol anticipated in the near future, in a realistic time frame, would have an adverse effect upon respiratory function.

[H D Kerr, et al. Environmental Research 26, 42-50 1981]

• Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group.

The Physicians' Health Study is a randomized, double-blind, placebocontrolled 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 less than 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 Jul 20;321(3):129-35. Comment in: N Engl J Med. 1989 Dec 28;321(26):1825-8. N Engl J Med. 1989 Jul 20;321(3):183-5.

• Randomised trial of prophylactic daily aspirin in British male doctors.

A six year randomised trial was conducted among 5139 apparently healthy male doctors to see whether 500 mg aspirin daily would reduce the incidence of and mortality from stroke, myocardial infarction, or other vascular conditions. Though total mortality was 10% lower in the treated than control group, this difference was not statistically significant and chiefly involved diseases other than stroke or myocardial infarction. Likewise, there was no significant difference in the incidence of non-fatal myocardial infarction or stroke–indeed, disabling strokes were somewhat commoner among those allocated aspirin. The lower confidence limit for the effect of aspirin on non-fatal stroke or myocardial infarction, however, was a substantial 25% reduction. Migraine and certain types of musculoskeletal pain were reported significantly less often in the treated than control group, but as the control group was not given a placebo the relevance of these findings was difficult to assess. There was no apparent reduction in the incidence of cataract in the treated group. The lack of any apparent reduction in disabling stroke or vascular death contrasts with the established value of antiplatelet treatment after occlusive vascular disease.

[Peto R, Gray R, Collins R, Wheatley K, Hennekens C, Jamrozik K, Warlow C, Hafner B, Thompson E, Norton S, et al. Br Med J (Clin Res Ed). 1988 Jan 30;296(6618):313-6.]

• Effects of stretching before and after exercising on muscle soreness and risk of injury: systematic review

Objective: To determine the effects of stretching before and after exercising on muscle soreness after exercise, risk of injury, and athletic performance.

Method Systematic review. Data sources: Randomised or quasirandomised studies identified by searching Medline, Embase, CINAHL, SPORTDiscus, and PEDro, and by recursive checking of bibliographies.

The review included randomised or quasi-randomised studies that investigated the effects of any stretching technique, before or after exercising, on delayed onset muscle soreness, risk of injury, or athletic or sporting performance. Studies were included only if stretching was conducted immediately before or after exercising. Studies reported in languages other than English were not included as translations were not available.

Main outcome measures: Muscle soreness, incidence of injury, athletic performance.

[Rob D Herbert, Michael Gabriel BMJ Vol 325 31 Aug 2002 bmj.com]

- Dust exposure and lung cancer in Quebec chrysotile miners and millers.
 - Liddell FD, McDonald AD, McDonald JC. Dust exposure and lung cancer in Quebec chrysotile miners and millers. Ann Occup Hyg. 1998 Jan;42(1):7-20.
 - Liddell FD, McDonald AD, McDonald JC. The 1891-1920 birth cohort of Quebec chrysotile miners and millers: development from 1904 and mortality to 1992. Ann Occup Hyg. 1997 Jan;41(1):13-36.
 - McDonald JC, Liddell FD, Dufresne A, McDonald AD. The 1891-1920 birth cohort of Quebec chrysotile miners and millers: mortality 1976-88. Br J Ind Med. 1993 Dec;50(12):1073-81.
 - McDonald JC, Liddell FD, Gibbs GW, Eyssen GE, McDonald AD. Dust exposure and mortality in chrysotile mining, 1910-75. 1980. Br J Ind Med. 1993 Dec;50(12):1058-72.

• The Nurses' Health Study

The Nurses' Health Study, established in 1976 by Dr. Frank Speizer, and the Nurses' Health Study II, established in 1989 by Dr. Walter Willett, are among the largest prospective investigations into the risk factors for major chronic diseases in women. http://www.channing.harvard.edu/nhs/

• Outcomes of pregnancy in a national sample of resident physicians

BACKGROUND. Physically demanding, highly stressful work during pregnancy has been reported to cause a variety of adverse outcomes. It has been difficult, however, to separate the effects of work from those of socioeconomic status.

METHODS. By means of a national questionnaire- based survey, we studied the outcomes of pregnancy during residency for 4412 women who graduated from medical school in 1985 and for (...), who served as controls.

[Klebanoff MA et al. 1990 Oct 11 , N Engl J Med pp 1040-5]

• Vasectomy and health. Results from a large cohort study.

In this xxxxxxx xxxxx study we identified, located, and, if living, interviewed 10,590 vasectomized men from four cities, along with a paired neighborhood control for each. The times between procedure data and interview or death ranged from under one to 41 years, with median equal to 7.9 years and with 2,318 pairs having ten or more years of follow-up. Participant reports of diseases or conditions that might possibly be related to vasectomy through an immunopathological mechanism were validated by direct contact with physicians and review of medical records.

Results of this study do not support the suggestions of immunopathological consequences of vasectomy within the period of follow-up. Except for epididymitis-orchitis, the incidence of diseases for vasectomized men was similar or lower than for their paired controls.

 $[{\rm Massey}\ {\rm FJ}\ {\rm Jr},\ {\rm et}\ {\rm al.}\ {\rm JAMA}.$ 1984 Aug 24-31;252(8):1023-9]

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- A xxxxxxxxxxx Study of Measles, Mumps, and Rubella Vaccination and Autism

It has been suggested that vaccination against measles, mumps, and rubella (MMR) is a cause of autism.

[K M Madsen, A Hviid, ... M Melbye N Engl J Med 2002;347:1477-82.]

• Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative xxxxxxxx xxxxxx xxxxxxxxx

CONTEXT: Despite decades of accumulated observational evidence, the balance of risks and benefits for hormone use in healthy postmenopausal women remains uncertain.

OBJECTIVE: To assess the major health benefits and risks of the most commonly used combined hormone preparation in the United States. DESIGN: ...

MAIN OUTCOMES MEASURES: The primary outcome was coronary heart disease (CHD) (nonfatal myocardial infarction and CHD death), with invasive breast cancer as the primary adverse outcome. A global index summarizing the balance of risks and benefits included the 2 primary outcomes plus stroke, pulmonary embolism (PE), endometrial cancer, colorectal cancer, hip fracture, and death due to other causes.

[Writing Group for the Women's Health Initiative Investigators. JAMA. 2002 Jul 17;288(3):321-33.]

 \bullet Innovations in health care: antiseps is as a case study*

Oliver Wendell Holmes / Ignaz Philipp Semmelweis / Joseph Lister / Florence Nightingale / Louis Pasteur

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